

ACTA OTO-LARYNGOLOGICA
SUPPLEMENTUM 309

THE AETIOLOGY OF PERCEPTIVE DEAFNESS

A Clinico-Pathological and Anatomical Study
of Temporal Bones and Brain Structures

BY
CARL CHRISTIAN HANSEN M.D.

ODENSE
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Denne afhandling er af det natur- og lægevidenskabelige fakultetsråd ved Odense Universitet antaget til offentligt at forsvares for den medicinske doktorgrad.

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PREFACE

The studies presented here were elaborated over a period of 11 years (1960–1971) during appointments in departments and institutes connected with The University of Aarhus, The University of Southern California, and The University of Odense.

The encouragement to commence working with the complicated subject – the aetiology of perceptive deafness came from Ole Bentzen, M.D., Ph.D., The State Hearing Rehabilitation Centre, Aarhus, who during my time in his department, and later on, inspired me and supported the efforts. For all this I am in great debt of gratitude. Audiometry Technician, Mrs. Annie Jentsch gave me able assistance in performing many of the audiometric evaluations, for which I extend my sincere thanks.

I am greatly indebted to my chief in the Department of Otolaryngology, Professor H. C. Andersen, M.D., Ph.D., The University Hospital of Aarhus, and the chief of the Department of Neurosurgery, Professor R. Malmros, M.D., Ph.D., The University Hospital of Aarhus, who both provided excellent working conditions for me and guided my efforts.

During the last four years of my stay in Aarhus, and later on during each phase of progress and realization of the many problems connected with my theme, the chief of Neuropathology, The University Hospital of Aarhus, Edith Reske-Nielsen, M.D., Ph.D., gave me invaluable support. Dr. Edith Reske-Nielsen is the co-author to three of the articles included in this monograph (the treatises A–C). Here she made the gross investigation of the brains plus the microscopy of brain sections. Too she assisted in the further elaboration of the comparative evaluation of the temporal bone and the brain findings. During the final compilation of the monograph she offered her assistance by counseling in some of the conclusions drawn from the collected findings of parts 1 and 2. Dr. Edith Reske-Nielsen has always given great consideration, sober criticism, and kind understanding to this project. The Department of Neuropathology she has endowed with a distinguished atmosphere of scientific enthusiasm, a never failing helpfulness and kindness, which it has been a special privilege to experience. For all this I am in great debt of thankfulness.

Mrs. Alice Strørup, Laboratory Technician in the Department of Neuropathology, Århus Kommunehospital, offered valuable and skilfull support during all the phases of this project, which is kindly acknowledged.

Professor Emeritus Willy Munck, former chief, Department of Pathology, Århus Kommunehospital, along with his assistants – especially Werner Petersen, Technical Assistant – offered their kind support by providing me with autopsy material.

Professor H. K. Kristensen, M.D., Ph.D. and his staff at the Temporal Bone Laboratory, Rigshospitalet, Department of Otolaryngology, Copenhagen, offered

their service by staining the temporal bone sections included in part 1 of this monograph; this I hereby acknowledge with special gratitude.

During the busy years at different departments in Los Angeles, the possibility of establishing a Temporal Bone Vessel Laboratory was made available for me especially by the aid of William F. House, M.D., Research Director, Otologic Medical Group. Funds were provided in part by the Board of Trustees, Los Angeles Foundation of Otology, for which I am extending my sincere thanks, especially to the President of the Foundation, Howard P. House, M.D. Doctor William F. House advised me in many of the steps during the practical elaboration of the thick, cleared section technique, he too gave me invaluable support and encouragement, inspiration, — and was a generous friend. The laboratory was installed in the Raulston Research Building under the kind supervision of Aldon Miller, M.D., chairman of the Department of Otolaryngology, the University of Southern California. For stimulation and practical help during this period I also express my appreciation to Clay R. Whitaker, M.D., Associate Professor, Department of Otolaryngology, the University of Southern California.

The Temporal Bone Laboratory, Otologic Medical Group, Head: Fred H. Linthicum, Jr., M.D., and George Kelemen, M.D., offered me valuable assistance in the decalcification process, which is hereby gratefully acknowledged. This appreciation should be extended also to the laboratory technicians.

Jack Urban, P.E., Urban Engineering Company helped in the construction of devices for the transillumination technique, by which it was made possible to undertake preliminary investigations of the vascular anastomoses from the labyrinth to the middle ear. It was a daily pleasure for me to work with him.

Antonio Mazzoni, M.D., Department of Otolaryngology, Ferrara, Italy, joined with me in the laboratory in Los Angeles one year after the onset of the project. He later on moved to the Department of Anatomy, the University of Odense. Dr. Mazzoni should be thanked for the enthusiasm, with which he cooperated on many problems in the temporal bone anatomy. He was most helpfull in working out technical details, in carrying material to Odense, and in participating in many professional discussions.

Cyril B. Courville, M.D., Professor of Neurology, Loma Linda University, contributed with his tremendous knowledge and understanding to the evaluation of pathological findings. I deeply regret that he did not see the completion of this monograph before his death; it was a sorrow for me that I did not experience the opportunity of cooperating with this noble and inspiring confrere in future projects.

The investigation was completed at Odense University, where Franz Bierring, M.D., Professor of Anatomy, generously supported the project by means of space, salary and equipment. Professor Bierring's good advice and kindness very often gave me great inspiration during my work in his institute. I also wish to express my thanks to all other members of his staff, among whom I am especially indebted to Laboratory Technician Mrs. Ingelise Rohleder, Laboratory Technician, Miss Julie Levinsen, and Medical Photographer E. Panton. Furthermore I want to acknowledge the helpfulness of Bent Collatz Christensen, M.D.

The Professor of The Institute of Pathology, A. Ringsted, M.D., Ph.D., gave me invaluable support by freely providing me with material, for which I am very thankful.

Otto Jepsen, M.D., Ph.D., Professor of Otolaryngology, The University Hospital of Odense, took a great interest in this research program. His kindness and soberness made it a daily pleasure for me to work in his department and discuss mutual scientific problems.

To Professor Horst Wullstein, M.D., Ph.D., University Clinic of Otolaryngology, Würzburg, Germany, I am very obliged for the generous interest which he took in this investigation. Our many inspiring dialogues, the invaluable practical help provided during publication procedures, and his personal magnanimity constituted a highlight in scientific experience.

Anita Engelbreth-Holm, M.T.F., translated this monograph. I hereby extend my sincere thanks for her assistance.

This project has been granted economical support from: Statens Lægevidenskabelige Forskningsråd, Copenhagen and P. Carl Petersen Fond, Copenhagen.

PREVIOUS PUBLICATIONS

The study here submitted represents abstracts of the following treatises:

- A. Cortical hearing loss in a patient with glioblastoma. Neuropathological analysis of a case. *Arch. Otolaryng.* 1963, 77: 461. (In collaboration with Edith Reske-Nielsen).
- B. Pathological studies in presbycusis. Cochlear and central findings in 12 aged patients. *Arch. Otolaryng.* 1965, 82: 115. (In collaboration with Edith Reske-Nielsen).
- C. Pathological studies in perceptive deafness. A patient with hydrops of the labyrinth. *Acta oto-laryng.* (Stockh.) 1963, suppl. 188: 162. (In collaboration with Edith Reske-Nielsen).
- D. Vascular anatomy of the human temporal bone. A preliminary report. *Ann. Otol. (St. Louis)* 1970, 79: 269.
- E. Vascular anatomy of the human temporal bone I: Anastomoses between the membranous labyrinth and its bony capsule. *Arch. klin. exp. Ohr.-, Nas.- u. Kehlk. Heilk.* 1971, 200: 83.
- F. Vascular anatomy of the human temporal bone II: Vascular anastomoses inside the labyrinthine capsule. *Arch. klin. exp. Ohr.-, Nas.- u. Kehlk. Heilk.* 1971, 200: 99.
- G. Vascular anatomy of the human temporal bone III: The vascularization of the vestibulo-cochlear nerve. *Arch. klin. exp. Ohr.-, Nas.- u. Kehlk. Heilk.* 1971, 200: 115.

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INTRODUCTION

According to the relevant literature, the aetiology of perceptive hearing loss, especially the loss experienced late in life, has been explained as a lesion involving peripheral as well as central sites in the auditory system. So far, however, systematic studies including a correlation of the clinical and pathological findings in the peripheral auditory organ have failed to demonstrate any parallelism between the degenerative changes involving the internal ear and the diagnosed loss of hearing (*Sporleder*, 1899; *Crowe et al.*, 1934; *Saxén*, 1952; *Schuknecht*, 1955). Consequently, these authors held that the aetiology of this type of hearing loss might include changes due to age in the cerebral auditory pathways and centres. *Matzker* (1958) and *Kirikae et al.* (1964), for instance, have observed such changes in the brain stem. Unfortunately, comparative studies of peripheral and central lesions in patients with well-defined perceptive deafness are not available.

During my term, from 1959 to 1960, in Statens Hørecentral in Århus (The State Hearing Centre in Århus (Head: O. Bentzen, M.D., Ph.D.)), I was inspired to embark on such a comparative clinico-pathological study of structures in temporal bones and brains. In patients whose past medical histories included episodes of heart failure or sequelae of cerebral apoplexy, the hearing loss seemed to be of a degree more severe than that otherwise observed in healthy individuals at equivalent ages. In the course of the ensuing study, the audiometric findings were evaluated and the degrees of the arteriosclerotic cerebral changes were determined; the study included bilateral arteriography of carotid vessels as well (performed in the Neurosurgical Department G of Århus Kommunehospital (University Clinic in Århus) (Head: R. Malmros, M.D., Ph.D.)). On the basis of these tests the severity of the cerebral lesions was found to be almost directly proportional to the hearing losses diagnosed by pure-tone audiometry. According to these purely clinical, preliminary studies (*Hansen*, 1961) it seemed as if hearing losses which develop late in life might be attributable to cerebral lesions. The author found it worth consideration to compare structures in temporal bones and brains and hence, exposed two groups of patients to audiometric examination, namely one group comprising 100 patients above the age of 65 years, and one group comprising 50 patients in the age group 20 to 60 years; – unpublished data. Autopsy was performed in 14 cases, and the temporal bones and brains excised on these occasions were exposed to study. The findings are discussed in Part 1 of the present monograph.

Gross inspection and microscopy of the brains were performed by Edith Reske-Nielsen, M.D., Ph.D., Head of the Department of Neuropathology, University Hospital, University of Århus.

These comparative studies of the degree of the pathological changes in the

various sections of the auditory system disclosed obvious discrepancies. For instance, the arterial system in the base of the skull might occasionally be a site of severe arteriosclerotic changes—even occlusion of the vascular lumen— while vessels as well as neural elements in the labyrinth apparently remained normal. This, however, is hardly compatible with the general concept according to which arteries of the labyrinth are end-arteries. By means of injections of contrast matter, the author tried consequently to clarify whether there might be a vascular connection between extracranial vessels via the osseous structures of the labyrinth to the vascular system in the labyrinth, in excess of the supply to the peripheral hearing organ via intracranial vessels.

The techniques used for such experimental injections into 43 temporal bones from man were elaborated by the author. The series comprise temporal bones derived from senile patients as well as from much younger individuals.

The findings obtained in these experiments are discussed in Part 2 of the present monograph.

On the initiative of, and in collaboration with, William F. House, M.D., Otolgic Medical Group, Los Angeles, the first part of the study was commenced; it was supported by grants from the University of Southern California, Department of Otolaryngology (Head: Aldon Miller, M.D.) and the Otological Medical Foundation in Los Angeles (Head: Howard P. House, M.D.). Later, the project has been completed in the Institute of Anatomy, Odense University (Head: F. Bierring, M.D.). One detail of practical interest (item 11, page 79) for the elaboration of the celloidine technique by which to study injected specimens was elaborated in cooperation with Antonio Mazzoni, M.D., Ferrara, Italy, who joined the laboratory one year after its establishment. Furthermore, he injected one colour "microphil" into ten of the temporal bones used for this study.

The monograph comprises two parts: a clinico-pathological and an anatomical-experimental, the object being to arrive at an explanation of some of the factors responsible for the development of perceptive deafness, in particular that of the type "pertaining to age".

PART 1

Clinical and Pathological Studies

The subject matter of Part 1 is the histological study of temporal bones and brains from patients who have been exposed to pure-tone audiometry, with a view to amplifying our present insight into the pathological basis of perceptive hearing loss associated with old age.

Chapters I, II, III, IV, and V are abstracts of treatises A, B, and C.

CHAPTER I

Material and Methods

The series comprise a total of 14 patients who are classified into the following groups:

A 43-year-old patient with cerebral tumour and fluctuating hearing capacity; treatise A: "Cortical hearing loss in a patient with glioblastoma".

Twelve senile patients, all of whom except one were above the age of 65 years; treatise B: "Pathological studies in presbycusis. Cochlear and central findings in 12 aged patients".

One 65-year-old patient with Ménière's syndrome; treatise C: "Pathological studies in perceptive deafness. A patient with hydrops of the labyrinth".

The techniques used for post-mortem inspection of brains and temporal bones and for the preparation of the histological specimens were identical in the three cited studies.

The patients were hospitalized in Århus Kommunehospital (University Clinic in Århus), or in departments attached, and died there during the period from 1961 to 1963. They had all been carefully examined, clinically as well as otologically; pure-tone audiometry at frequencies of 250, 500, 1000, 2000, 4000, and 8000 cycles per second had been performed in all cases.

Organs and brains from all patients were inspected and the temporal bones were excised.

The temporal bones were fixed in 4 % neutral formalin for at least one week and forwarded to the Temporal bone Laboratory of Professor H. K. Kristensen, Rigshospitalet (University Clinic, Copenhagen). Using the technique recommended by *Kristensen* (1949), the preparations were decalcified for about four or five months in a buffer solution composed of equal portions of 8 n formic acid and 1 n sodium formate, pH 2.2. The decalcified specimens were embedded in celloidin and cut in the horizontal plane in serial sections, the thickness of 15 micron.

Every 10th section was stained with Ehrlich's haematoxylin-eosin. Selected sections were exposed to the following specific stains: Nissl-substance stain using Anthracene blue, pH 2; myelin sheath stain combined with connective tissue stain according to Kultschitzky + van Gieson; axis cylinder stain, using Bodian's method; and periodic acid-Schiff (PAS) according to McManus.

The brains were fixed for at least three weeks in 4 % neutral formalin.

A central block comprising cerebrum, brain stem, and cerebellum was removed in order to follow the acoustic pathways histologically. Anteriorly the block was limited by the optic chiasm, laterally by the hippocampal gyri, and posteriorly by the cerebellum.

In the course of dissection of the block, the following regions were selected with special reference to a study of the acoustic pathways and nuclei:

1. The site of transition between the pons and the medulla oblongata, including the acoustic nerves.
2. The pons at the site of the trigeminal nerves.
3. The mesencephalon, including the inferior colliculus.
4. The upper portion of the mesencephalon, including the medial geniculate body.
5. Matter from both auditory centres: the transverse gyri and the central portion of the superior temporal gyrus, together with
6. Supplementary tissue specimens from other parts of the brain beyond the auditory pathways and centres.

The specimens were cut in sections, the thickness of 7 micron.

In excess of the routine stains such as haematoxylin-eosin, van Gieson, gallo-cyanin-chromalum (Einarson) and Mahon, the following specific stains were used: axis cylinder stain according to Davenport; modified McManus stain; and toluidine blue.

Note: If not otherwise stated, the figures are designated in accordance with those in the treatises.

CHAPTER II

Neuropathological Analysis of the Temporal Bone and the Brain in a Patient with Glioblastoma and Fluctuating Hearing Capacity

According to a series of previously published studies (*Grahe*, 1932; *Brunner*, 1935; *Walker*, 1951; *Nielsen & Berryman*, 1952; *Saltzman*, 1952; *Drake & McKenzie*, 1953; *Greiner et al.*, 1953, 1956; *Spiegel & Wycis*, 1953; *Thiébaud et al.*, 1957; *Wycis et al.*, 1958; *Bentzen*, 1961), audition of pure tones may vary parallel with pathological changes in the brain.

The present chapter, which is a synopsis of treatise A, outlines briefly the most important data in the case history together with the clinical findings, in particular the audiometric findings, in a 43-year-old man whose hearing fluctuated parallel with pathological processes in the brain; the lesions were partly attributable to the neurosurgical measures performed. The patient died of pulmonary embolism. The most important pathological findings are discussed and an attempt is made to have the clinical and pathological findings correlated.

The patient was admitted to the neurosurgical department G in November 1959 on account of progressing headaches associated with pressure exacerbation and explosive vomiting. The clinical examination failed to reveal any anomalies. Papillary oedema of 1 dioptré and haemorrhages of a marbled pattern involving the background of the eye were manifest.

Audiometry of the 43-year-old patient showed that his hearing still was normal (fig. 1).

The caloric reactions to irrigation with water at 30° C were normal. Ventriculography disclosed a space-filling process anteriorly in the right cerebral hemisphere and surgery exposed a tumour, measuring about $3 \times 8 \times 6$ cm, in the posterior portion of the frontal region to the right; it was questionable whether surgery had been sufficiently radical at medial and profound sites towards the basal ganglia. The histological diagnosis was established as: glioblastoma (signed: Edith Reske-Nielsen).

Four days after surgery the patient managed to co-operate satisfactorily at the audiometry carried out in the ward. The audiogram (fig. 1, corresponding to fig. 2 in treatise A) was comparable with that of a "presbycusis" hearing curve obtained in cases of 75-year-old patients, according to the standard established by *Johansen* (1943). At this stage, a moderate, left-sided, central facial paresis occurred together with slight paresis of the left arm.

Six days after surgery, audiometry was repeated. The patient's hearing had improved a little (fig. 1, corresponding to fig. 4 in treatise A).

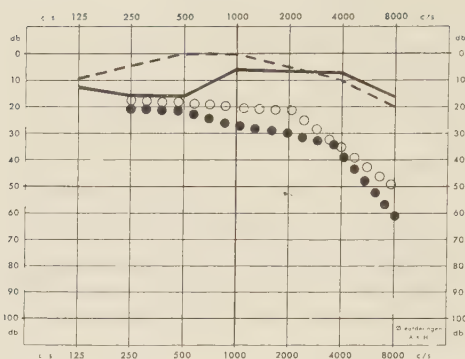


Fig. 1. Hearing curves depicting the fluctuating audition, bilaterally symmetrical, in the patient discussed in chapter II.

Fully drawn line,	= prior to	first surgical intervention
Dotted line,	= four days after	— — —
Circles,	= six days after	— — —
Dashed line,	= five months after	— — —

Five months later, the patient was seen in his own home in order to have an audiometric follow-up. He felt quite well and it was his intention to resume work. His only complaint was some trouble with the fingers of his left hand which he was unable to control. The audiogram showed normal conditions (dashed line in figs. 1 and 2, corresponding to fig. 6 in treatise A).

Eight months and two weeks after surgery, the patient was re-admitted to the department on account of a moderate loss of strength in the left extremities and an increased demand for sleep. The patient did not realize his own condition, in particular, he did not complain of hearing failure.

Clinical symptoms involving the right side of the brain were demonstrable. Bilateral arteriography of the carotid arteries revealed recurrence of the tumour in the right cerebral hemisphere and ingrowth into the left cerebral hemisphere. Ophthalmological examination showed papillary oedema of 2 dioptries while the otological findings were normal. According to the audiogram, his hearing had deteriorated during the three-month-interval, particularly his perception of tones in the high-frequency range (fig. 2, corresponding to fig. 7 in treatise A).

Partial removal of the glioblastoma was performed, including resection of the entire frontal lobe on the right side and excision of large quantities of tumour tissue at the site of the foremost parietal lobe, but radical surgery was not practicable.

Transistorized audiometry was carried out in the ward 12 days after surgery on which occasion the patient managed to co-operate satisfactorily (fig. 2, corresponding to fig. 8 in treatise A) although he was still somewhat apathetic. The curve depicting the symmetrical hearing loss was found to equal that otherwise obtained in cases of 75-year-old patients, according to the standard established by Johansen (1943). In fact, the patient's hearing was just as good as it had been when he, eight months earlier, had been suffering from cerebral oedema (figs. 1 and 2).

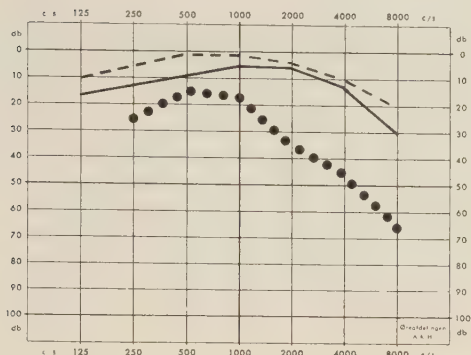


Fig. 2. Hearing curves depicting the fluctuating audition, bilaterally symmetrical, in the patient discussed in chapter II. (1): Curve obtained by audiometry carried out in the patient's home (dashed line); (2): curve obtained prior to the second surgical intervention indicated by the tumour (fully drawn line); (3): curve obtained while cerebral oedema, provoked by the repeated surgery, was in evidence (dotted line).

Ophthalmological examination on the same day revealed papillary oedema of 2 dioptries on both eyes.

The patient died suddenly two days after the last audiometric examination.

Immediately upon death, the brain was fixed *in situ* in a 4 % solution of neutral formalin.

Post-mortem inspection of the organs revealed a large pulmonary embolism, but otherwise normal findings.

The brain and the left temporal bone were removed.

Microscopy of the left temporal bone: normal conditions (cf. treatise A).

Gross inspection of the brain: A defect, measuring $8 \times 8 \times 6$ cm, was demonstrable in the right frontal lobe, extending upwards into the adjoining portion of the right temporal lobe which was lined by brain tissue infiltrated by the tumour. The infiltration spread to the striate bodies, the internal capsule, and the anterior portion of the right thalamus. Through the corpus callosum the growth penetrated into the left frontal lobe at which site the infiltration extended medially, and in front of, the anterior horn.

Microscopy of the brain: The histological findings in the acoustic pathways, the nuclei, and in the cortical hearing centres have been discussed in detail in treatise A and consequently, the pathological findings shall merely be outlined here, classified according to degrees of severity; also the influence of the latter on the hearing is evaluated.

I. Chronic lesions which are presumed to suppress completely functions in the regions concerned:

1. Malacias localized to the right cortical hearing centre.
2. Disappearance and degeneration of the white substance in the right temporal lobe.
3. Atrophy and degeneration of the right inferior colliculus.
4. Right-sided chronic degeneration of the white substance in the brain stem.

II. Acute lesions which are presumed to impair functions in the areas concerned:

1. Oedema and degeneration involving the left cortical hearing centre.
2. Severe, acute degeneration of the white substance in the left temporal lobe.

III. Lesions localized to other pathways and nuclei in the brain stem were small only and may not have exerted any clinically demonstrable influence on the patient's hearing; it should be particularly stressed that the chronic and acute lesions were negligible in the right and left ventral and dorsal cochlear nuclei, in the trapezoid body, in the left inferior colliculus and in the medial geniculate body on either side.

Discussion and Conclusion

Mettler et al. (1934) demonstrated in experiments on dogs that extirpation of the cortical hearing centre in one hemisphere did not affect the hearing essentially, whereas destruction involving both hemispheres would be responsible for a hearing loss of 70–75 decibel at a frequency of 1000 cycles per second (c.p.s.). Furthermore, this author observed that the acoustic value of crossed and non-crossed pathways in the brain stem was identical since one aspect of the brain stem together with the ipsilateral cerebral hemisphere might be injured without affecting the hearing capacity, if only the trapezoid body was preserved.

In previous studies by, for instance, *Nylén* (1939), *Lemoyne* (1944), *Bocca et al.* (1955), *Carmichael et al.* (1956), *Goldstein* (1961), and *Maspétiol et al.* (1961), human audition was found to remain uninfluenced by lesions involving only one cerebral hemisphere. The entire tone range may remain audible even after hemispherectomy (*Dandy*, 1937).

Henschen (1920) did not observe loss of hearing in any of his 14 patients with lesions involving both hemispheres but an intact temporal lobe on one side.

On the other hand, some reports have been concerned with bilateral lesions localized to the transverse gyri or the white substance in both cerebral hemispheres in which cases the hearing capacity apparently was extinct (*Strohmayer*, 1901; *Campbell*, 1905; *Henschen*, 1916–1918, 1920; *Fraser & Nelson*, 1928).

As regards the patient discussed by *Fraser & Nelson*, both cochleae had been inspected simultaneously. The right cochlea was found to be normal while sequelae after a severe inflammation of the middle ear on the other side were in evidence.

Special interest is attached to the reports on patients with normal hearing who had experienced previous episodes of cerebral apoplexy, but lost their hearing later after repeated vascular episodes. Five case histories of this type are available; some of the patients were young, others were elderly individuals. The apoplectic episodes were attributable to embolism following endocarditis or mitral stenosis, to thrombosis in connection with cerebral arteriosclerosis, or, in one case, to haemorrhages in cerebral hydatid cysts. All of these patients survived for a couple of weeks after the vascular episode which had been responsible for their hearing

loss. In the cases described by *Sérieux & Mignot* (1901) and by *Bramwell* (1927), post-mortem inspection of the brains exposed "extensive destructive changes in the temporal lobes on either side". The patient described by *Mott* (1907) presented severe lesions localized to all transverse gyri, including the white substance on one side, while the pathological changes in the other hemisphere exclusively were localized to the cortex in the hearing centre. *Misch* (1928) observed that the lesion in his patient was localized only to the anteromedian part of the superior temporal gyrus of one hemisphere while the transverse gyri on the other side were totally destroyed. Finally, the extensive pathological, bilateral changes in the internal capsules involved also the acoustic radiation. In contrast, the cerebral cortex was found to remain normal in the deaf patient described by *Clark & Russell* (1938).

The above cited studies seem to indicate that the hearing capacity in man remains uninfluenced by unilateral hemispheric lesions whereas it will be extinct in patients in whom destructions involve the acoustic areas in both cerebral hemispheres. In the patient here discussed, the destruction of the right hearing centre may have been due to the severe oedema previously provoked by the tumour which involved the right cerebral hemisphere. Furthermore, ingrowth of the tumour into the right internal capsule may have been responsible for the severe right-sided, chronic degeneration of the brain stem, affecting in particular the efferent pathways. On the other hand, the degenerative changes in the trapezoid body and in the attached nuclei were rather mild, thereby suggesting that these were still functioning; this is commensurate with the clinical findings in the patient during intervals when cerebral oedema was absent and the patient's hearing on both ears was normal. The latter is in accord with findings obtained by *Mettler et al.* (1934) in experiments in which they destroyed one hearing centre together with the ipsilateral portion of the brain stem; the trapezoid body remained intact (fig. 3, corresponding to fig. 18 in treatise A).

Throughout the two postoperational periods in which the cerebral oedema was manifest, *also the left hemisphere* was partly out of action; in other words, both hearing centres were compromised; consequently, the patient's hearing failed, in particular his hearing of sounds in the high-frequency range (fig. 4, corresponding to fig. 19 in treatise A).

The patient died of acute pulmonary embolism after the second surgical intervention, at a time when the cerebral oedema was manifest and the hearing loss clinically reminded of that observed by *Johansen* in a series of normal, 75-year-old patients (*Johansen*, 1943); considered from a patho-anatomical point of view, the brain which was fixed *in situ* was in a condition like that observed at the audiometric examination when audition of pure tones had been lost because an acute, diffuse, cerebral oedema had been added to the chronic pathological lesions; consequently the left hearing centre had been blocked; the right hearing centre had been destroyed at an earlier stage (fig. 4, corresponding to fig. 19 in treatise A).

It is worth noticing that the acute changes of the brain stem were less marked than those of the cerebral hemisphere and that the left temporal bone remained intact.

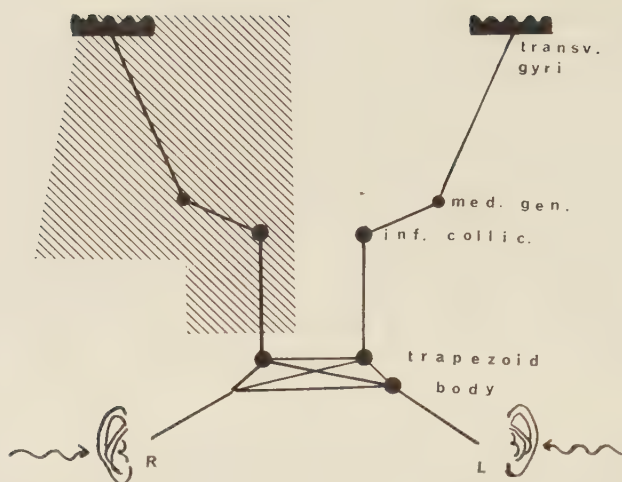


Fig. 3. The patient discussed in chapter II: Sketchy representation of localizations of the chronic pathological processes in relation to the cerebral auditory pathways and centres, hatched areas representing the pathological processes.

It seems reasonable to conclude on the basis of these clinical and pathological facts that the patient's loss of hearing, particularly his failing perception of tones in the high-frequency range, to a lesser degree of those in the low-frequency range (similar to features encountered in 75-year-old patients with presbycusis) may have been provoked by the recurring oedemas in the cerebral hemispheres. In other words, the hearing capacity is seen to fluctuate parallel with pathologically changing conditions in the brain.

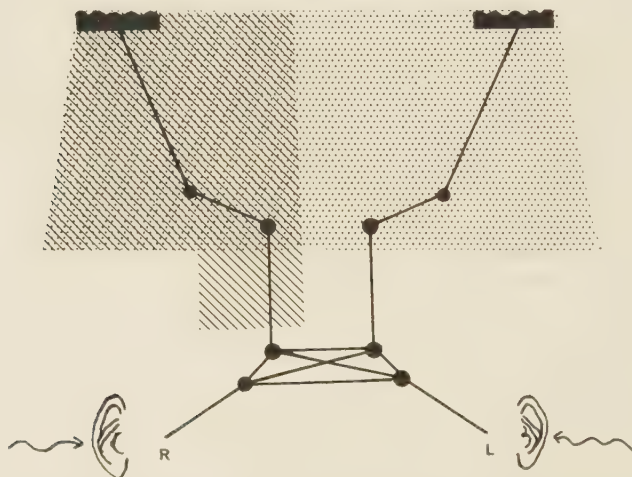


Fig. 4. The patient discussed in chapter II: Sketchy representation of localizations of the chronic (hatched area) and acute (dotted area) pathological processes in relation to the cerebral auditory pathways and centres.

CHAPTER III

Previous Studies of Senile Changes Involving the Peripheral Auditory Organ and the Central Auditory Pathways

The clinical findings in cases of perceptive hearing loss in old age are generally known, but the patho-anatomical factors responsible for the impaired hearing are much discussed, this applies to localization of lesions in and round about the peripheral auditory organ and the central auditory pathways as well as to the aetiology of these lesions.

Numerous studies are available in which audiometric findings have been collated with those obtained in patho-anatomical studies of the labyrinth.

Studies concerning the state of the central auditory pathways and centres in patients whose hearing is impaired due to age, however, are less numerous.

The literature on these topics is comprehensive. The author has tried to select publications with relevance to the individual structures, fully realizing that there may be some overlapping.

A: Changes involving the epithelial cochlear elements

Descriptions of the following lesions are on record: Flattening and degeneration of the organ of Corti, reduced number, or complete absence, of hair cells and flattening of the supporting cells. Occasionally the tectorial membrane may be thin and be incorporated into the formation of synechia; Reissner's membrane has often been seen to adhere downwards over the organ of Corti (e.g. *Saxén*, 1952; *Jørgensen*, 1961).

According to the selected publications, the lesions may be attributable to: (1) Angiosclerosis involving the internal ear; (2) failing nutrition of the organ of Corti via the endolymph; (3) atrophy due to old age; (4) secondary atrophy owing to lesions of the spiral ganglion of the cochlea; and (5) changes to occur at terminal stages or after death.

re (1) The incidence as well as the spread of angiosclerotic lesions increase parallel with age; this is particularly true of lesions at the site of the vascular stria. According to *Fabinyi* (1931), *Crowe et al.* (1934), *Schuknecht* (1955), and *Jørgensen* (1961), they occur uniformly throughout all coils. A parallelism between degrees of vascular changes and degeneration of the organ of Corti is not demonstrable (*Crowe et al.*, 1934; *Saxén*, 1952; *Schuknecht*, 1955; *Jørgensen*, 1961). According to *Covell and Rogers* (1957), stria vessels of normal appearance may be encountered in areas displaying complete atrophy of the organ of Corti.

re (2) According to modern physiological and histochemical studies, the organ of Corti is supplied through the endolymph secreted from the vascular stria, cf. *Jørgensen* (1962). It is open to discussion, however, whether a reduced secretion of the endolymph, due to pathological processes in the vascular stria, may be responsible for the deafness to develop in old age since, as already mentioned, there is no correlation between the pathological processes in the vascular stria and those in the organ of Corti.

re (3) *Schuknecht* (1955) declared that senile atrophy of the cochlea was the otological manifestation of processes due to age which are in evidence in all tissues throughout the body. Such atrophy has been found to begin in the basal cochlear coil and to include all structures of the middle scale, for instance, the afferent and efferent fibres.

re (4) The epithelial changes may be secondary to the disappearance and degeneration of nerve cells in the spiral ganglion of the cochlea. This postulation is corroborated by the fact that epithelial changes rarely are encountered in cochlear areas where ganglion cells are intact (*Saxén*, 1952; *Covell and Rogers*, 1957). *Schuknecht* (1953) managed to destroy the neural elements in cats, escaping a development of secondary lesions of the organ of Corti.

re (5) Finally, the histologically demonstrable changes in epithelial elements may have been provoked by such diseases as were responsible for the death of the patients, or by changes to develop at terminal stages; also the fixation time and fixation techniques may play some role (*Lange*, 1937).

In addition to the lesions localized to the middle scale, *Mayer* (1919) observed a thickening of the basilar membrane at which site calcareous deposits were in evidence, mainly in the basal coil. Such lesions, however, have later been seen also in patients whose hearing was normal (*Crowe et al.*, 1934).

According to *Saxén* (1952) and *Fleischer* (1956), the above mentioned histopathological changes are not constant findings in the epithelial elements of the cochlea in elderly patients exclusively; the same feature has actually been encountered even in 7-year-old patients by *Jørgensen* (1961).

Hence, if these histopathological changes, which all were demonstrable by histological routine section and staining technique, were collated with those observed by audiometric examination of patients with presbycusis, it seemed highly improbable that the demonstrated pathological changes had been exclusively responsible for the loss of hearing. The reason may be that the clinical procedures, the histological and the biochemical techniques were not sufficiently delicate to disclose such correlation. Accordingly, a few studies in which these more advanced techniques were used shall be cited.

Using the monaural balance test which according to *Pestalozza and Shore* (1955) represents a standard of the functioning capacity of hair cells, these authors found values to be within the normal range in one half of all individuals in their series of patients with presbycusis.

Ruben (1963) found the cochlear microphonic potential (C.M.) to be within normal range in the basal coil in an elderly patient whose deafness to tones in the high-frequency range was of the classic presbycusis type. According to the

investigation, this indicates that functions of hair cells were fair at cochlear sites where high-frequency tones are perceived.

In a study of cochleae from elderly patients, *Bredberg* (1968) demonstrated by phase contrast microscopy of cochleae perfused with osmic acid that the disappearance of hair cells might be of different importance in the individual coils. At apical sites there tones in the frequency range 250 cycles per second are presumed to be perceived, the loss of hearing of tones in this range did not exceed 40 decibel, even though up to 50 % or 75 % of the external hair cells had disappeared. Conversely, in areas where tones in the range 8000 cycles per second are presumed to be perceived, a relatively smaller loss of external hair cells might result in a hearing impairment of a more severe degree. The author failed to demonstrate, however, whether the *pro rata* loss of *internal* hair cells might be correlated with the loss of hearing of tones in the high frequency range.

Such lacking correlation between degrees of degenerative changes in the organ of Corti and the functioning capacity of the latter has been observed also in guinea pigs by *Schnieder and Janzer* (1969). These authors induced lesions of hair cells by means of the so-called "white noise". As a standard of the degenerative changes, the lactose concentration in the perilymph was analysed and the results collated with the measured cochlear microphone potential were determined. Thus, the authors were able to demonstrate that even a considerable loss and degeneration of hair cells in the frequency range 4000 cycles per second did not reduce the cochlear microphone potential in the area of the basal cochlear coil.

On the basis of the above cited studies, it may be reasonable to presume that the degenerative changes in the epithelial elements of the cochlea hardly can be exclusively responsible for the hearing loss applying to tones in the high-frequency range, a loss which otherwise is typical in cases of presbycusis.

*B: Changes involving the vessels of the temporal bone and the
vessels of the circle of Willis*

Vascular changes in the membranous portion of the cochlea are hardly contributory to a development of presbycusis. As previously mentioned, any parallelism between degrees of angiosclerosis in the vascular stria and degeneration of the organ of Corti is not in evidence and the same applies to vessels in the modiolus. Besides, the pathological changes involving the cochlear vessels were not directly correlated with the degenerative lesions in the spiral ganglion of the cochlea. (*Crowe et al.*, 1934; *Saxén*, 1952; *Schuknecht*, 1955; *Covell and Rogers*, 1957).

As regards the vascular changes involving the osseous capsule of the labyrinth, whether or not of any importance, *Gussen* (1968, 1969) ascertained, on the basis of conventionally stained celloidin sections, that the vascular supply apparently remained satisfactory even in very old subjects; in fact, it did not deviate much from that observed in young subjects. In patients with presenile arteriosclerosis, however, a development of thrombi in these vessels seemed to be more common (*Gussen*, 1969).

It is still open to discussion whether vascular changes involving the peripheral auditory organ may be correlated with changes in the cerebral vessels and, likewise, whether changes in the circle of Willis may be correlated with those in vessels running through the internal auditory canal.

Saxén (1952) observed angiosclerosis in vessels of the internal ear although coincident lesions of vessels in the internal auditory canal and those at the base of the brain were absent; in renal vessels, however, arteriolosclerosis was in evidence. On the other hand, *Jørgensen* (1961) declared that there might be a certain correlation between vascular changes in the vascular stria and those in the cerebral vessels, in particular in those at the base of the brain. On the basis of findings in a series of old patients, *Ishii* (1967) concluded that pathological changes in the basilar arteries, including the anterior inferior cerebellar arteries and those in the internal auditory canals, need not be correlated with lesions affecting the various structures of the internal ear.

In a study of a series of senile patients, *Fabinyi* (1931) compared the audiometric findings with the pathological processes in the large cerebral arteries. There was apparently some correlation between loss of hearing of tones in the high-frequency range and degrees of cerebral arteriosclerosis, but the relation between the loss of hearing of tones in the high-frequency range and changes in internal auditory canal vessels was less clear-cut.

C: Histopathological changes involving the spiral ganglion of the cochlea

Disappearance and degeneration of ganglion cells in the spiral ganglion of the cochlea are mainly demonstrable in the basal coil and represent the patho-anatomical process most constantly encountered in the labyrinth of elderly patients (*Crowe et al.*, 1934; *Saxén*, 1952; *Schuknecht*, 1955; and *Jørgensen*, 1961). According to *Fleischer* (1956), these lesions were the only ones to intensify parallel with advancing years; consequently he suggested that the neural changes might be solely responsible for the development of presbycusis.

Fabinyi (1931) and *Crowe et al.* (1934) have declared that degrees of changes in the ganglion cells of the basal coil might be correlated, though not absolutely, with the degrees of hearing loss applying to tones in the high-frequency range. In patients whose hearing was severely impaired, *Crowe et al.* (1934) and *Saxén* (1952) observed, however, that pathological processes involving the spiral ganglion might occasionally be of moderate degree.

In patients whose hearing is normal and who perceive tones in the high- as well as the low-frequency range, the percentage of damaged ganglion cells in the basal coil has been differently calculated by the individual authors; for instance, it has been found to range at 50 (*Crowe et al.*, 1934), at 75 (*Schuknecht*, 1955), even up to 80 (*Citron et al.*, 1963).

In a series of patients with presbycusis, *Saxén* (1952) observed that the percentage of degenerated nerve cells in the basal coil often might range below 50, while the percentage of ganglion cells in the middle and apical coil generally was

within normal range, even though perception of tones in the low-frequency range was found to vary greatly from patient to patient.

Obviously, a loss of hearing need not be correlated with a degeneration of neural elements, whether in basal, middle, or apical coils. Hence, it seems highly improbable if patho-anatomical lesions in the spiral ganglion were solely responsible for a development of presbycusis.

"The reason why the atrophic change selects the basal end is as great a mystery to me as the process of ageing itself" (*Schuknecht, 1955*).

Evidently, such changes in the spiral ganglion need not be secondary to a degeneration of the efferent pathways in the cochlea and, in fact, atrophic ganglion cells were not in evidence several weeks after bisection of the olivo-cochlear bundle (*Rasmussen, 1953*).

*D: Degeneration of the acoustic nerve throughout the tractus
spiralis foraminosus and the internal auditory canal*

Sërçer and Krmpotić (1958) observed some hyperostotic lesions at the site of tractus spiralis foraminosus, mainly involving the area where nerve fibres emerge from the basal coil. These findings may explain to some extent why perception of high tones may be impaired in old age, although other authors have failed to confirm the phenomenon.

According to *Crowe et al. (1934)*, the patho-anatomical lesions involving the cochlear nerve throughout the internal auditory canal may be of a degree more pronounced than that of the degenerative changes in the organ of Corti.

It remains obscure, however, whether such changes may be responsible for the loss of hearing in old age. *Neff (1947)* found that tones in the high-frequency range were imperceptible to experimental animals if more than 50 % of all fibres in the cochlear nerve had been bisected; in contrast, *Schuknecht and Woellner (1953)* who destroyed 75 % of this nerve in cats, avoided injuring the hearing.

In patients with acoustic neurinomas, severe degeneration of the cochlear nerve need not be associated with impaired perception of pure tones (*Schuknecht and Woellner, 1955; Jerger, 1960; Citron et al., 1963; House, 1968*).

It does not appear from the above cited studies, however, whether the histopathologically demonstrable lesions were localized to the peripheral (Schwann's) or the central (glial) part of the cochlear nerve.

Thus, it can be established that many investigators have pointed to the fact that the pathological changes of structures in the temporal bone are not exclusively responsible for a loss of hearing late in life.

*E: Pathological processes involving the cerebral
auditory pathways and centres*

Reports concerning the status of the auditory areas in the brains of patients with presbycusis are scarce.

According to *Scheidegger (1963)*, several types of diffuse, degenerative lesions

might occur in brains of presenile or senile patients, for instance, cerebral arteriosclerosis, senile atrophy, Alzheimer's syndrome, Pieck's disease, and the so-called "presenile spongy cerebral atrophy". There is reason to suppose that similar lesions may be encountered also in the cerebral auditory pathways and centres.

On the basis of findings in studies of the pathological processes involving the peripheral auditory organ, *Sporleder* (1899), *Crowe et al.* (1934), *Saxén* (1952), *Schuknecht* (1955), and *Ishii* (1967) failed to provide a sufficiently reliable explanation of the auditory lesions in patients with presbycusis; consequently they postulated that degenerative lesions in old patients also might involve the more centrally localized areas. This postulation was confirmed by *Kirikae et al.* (1964) who, in brains from 11 senile patients, found degeneration of ganglion cells in the ventral cochlear nucleus, in the superior olivary nucleus, in the inferior colliculus, and in the medial geniculate body.

The present author has not been able to procure studies including detailed data concerning the correlation of the hearing capacity in man and the cortical processes, if any, involving the auditory centres in the cerebral hemispheres.

Finally, reports concerning the histopathologically demonstrable processes in the temporal bones and brains of senile patients with presbycusis are not available.

CHAPTER IV

Analysis of the Pathological Processes Involving the Peripheral Auditory Organ and Central Pathways in Twelve Senile Patients Whose Loss of Perceptive Hearing was Verified

As mentioned in chapter III, numerous authors have discussed the patho-anatomical processes involving the cochlea as well as the central auditory pathways, processes which may have been responsible for the loss of hearing in old age; the authors concerned have correlated the loss of hearing with pathological processes localized exclusively to cochlear structures or to sites within the central auditory pathways and centres.

In a further attempt to define the patho-anatomical factors responsible for the loss of hearing in old age and to localize the origin, or origins, of such loss, a parallel has been drawn between the findings obtained by audiometry and the pathological lesions of the central auditory pathways and lesions of the temporal bone structures. As far as the author is aware, this type of study has not yet been performed.

According to patho-anatomical criteria, the 12 patients comprised in the series can be classified into four groups of 8, 2, 1, and 1 patients. The patients concerned have previously been discussed in treatise B of which an abstract follows:

Group I. 8 patients

The past medical histories of these eight patients were identical which applies also to the audiological and patho-anatomical findings, though individual variations might be encountered:

Table 1 represents a survey of findings by audiometry, incidence of intercurrent diseases, causes of death, and autopsy findings in organs from the eight patients; the series comprised four men and four women at ages above 80 years except one who was only 66 years old.

The blood pressure was normal according to age in all patients except in the patient classified into group III.

The past audiological histories contained no data which might explain why these patients had lost hearing; indeed patients nos. 3 and 5 had experienced left sided otitis media while the remaining six patients had perceptive deafness, presenting symmetrical hearing curves (fig. 5, corresponding to figs. 15–22 in treatise B).

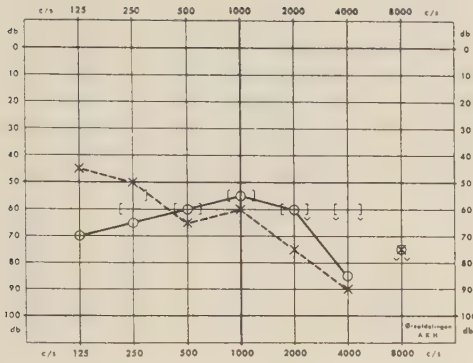
The average value of intelligibility thresholds in the ranges 250, 500, and 1000 cycles per second, i.e. the low-frequency ranges, varied from 10 decibel to 60 decibel. As regards the high-frequency range, audition was severely impaired in all

Table 1. *Audiological Examination*

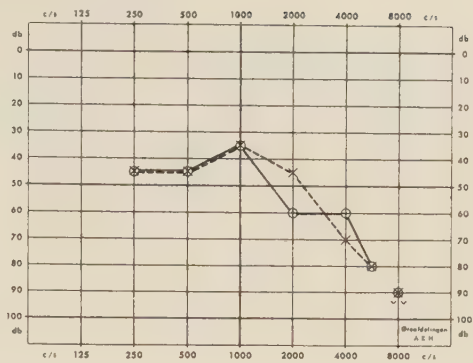
Group	Age	Sex	B. P.	Low-frequency mild < 40 medium > 40	Highest frequency severe > 60	Audiology prior to death	Cause of death	Other diseases	
I	(1)	86	♂	160/80	severe	extinct	14 months	Broncho-pneumonia	Arteriosclerosis
	(2)	82	♀	175/70	medium	extinct	60 days	Pulmonary embolism	Arteriosclerosis
	(3)	91	♀	170/80	medium	severe	24 days	Coronary occlusion	Arteriosclerosis
	(4)	80	♀	130/90	medium	severe	6 years	Coronary occlusion	Arteriosclerosis and leukaemia
	(5)	89	♂	145/100	medium	extinct	3½ years	Cerebral apoplexy	Arteriosclerosis
	(6)	83	♀	110/80	mild	severe	8 days	Pulmonary embolism	Arteriosclerosis and tuberculosis
	(7)	66	♂	105/60	mild	severe	2½ years	Carcinoma of the gall bladder	Arteriosclerosis
	(8)	88	♂	180/90	medium	extinct	18 days	Pulmonary embolism	Arteriosclerosis and cancer of the caecum
	(9)	80	♂	160/100	mild	severe	12 days	Croupous pneumonia	Arteriosclerosis
	(10)	79	♂	140/80	mild	extinct	1 year	Coronary thrombosis	Arteriosclerosis
	(11)	60	♂	240/130	mild	severe	2 years	Cerebral apoplexy	Arteriosclerosis
	(12)	69	♂	145/85	mild/ extinct	severe/ extinct	6 years	Acute Pyelonephritis	Arteriosclerosis

Patients discussed in chapter IV.

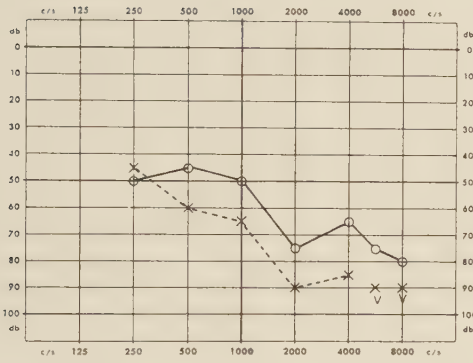
Pathological findings in temporal bones.



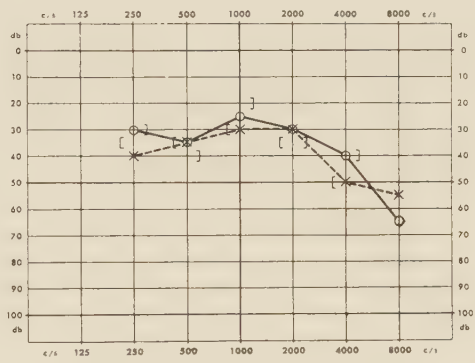
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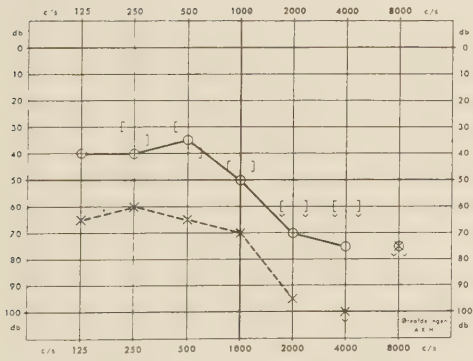
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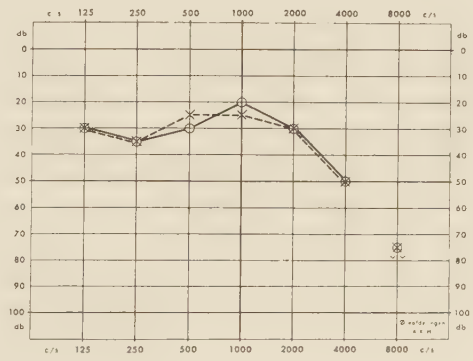
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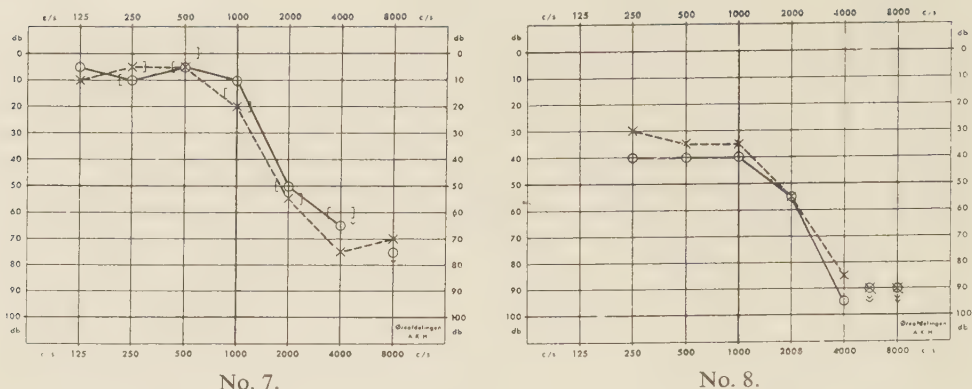


Fig. 5. Audiograms from the patients in group I (nos. 1-8, table 1).

patients. Discrimination losses in five patients were in the range: moderate to severe.

Vestibular irrigation, using water at about 20-30° C, gave normal and uniform reactions in all patients.

Four patients died of pulmonary diseases, two died of coronary sclerosis, one died after an apoplectic attack, and one died of metastases to the liver from a carcinoma of the gall bladder.

Autopsy inspection of organs disclosed severe arteriosclerotic lesions in all cases.

The pathological findings in the temporal bones were of identical nature in all patients although the intensity of the degenerative lesions might vary individually, (table 2).

The middle ear was of normal appearance in all but two patients, nos. 3 and 5, in whom the left ossicles were sites of severe osteitic lesions; adherances through the middle ear were broad and the tympanic membrane had thickened.

In another patient, no. 8, a cholesteatoma, not involving the ossicles, was in evidence, i.e. a "cholesteatoma *in situ*".

All structures in the middle scale, i.e. the vascular stria, the sulcus cells, and the organ of Corti, were found to be deformed and flattened. Changes varied from coil to coil, from section to section, and from the right to the left temporal bone in one and the same patient. Especially the appearance of the organ of Corti varied; in most sections it was hardly recognizable, while structures appeared rather well-preserved in other sections from the apical coil, the middle coil, and the basal coil. The tectorial membrane was displaced in relation to the organ of Corti while Reissner's membrane in many sections seemed to adhere downwards over the organ. Lesions in the organ of Corti appeared to be uniformly dispersed throughout all coils.

The basilar membrane had not thickened appreciably in any of the patients, particularly not at the site of the basal coil; any calcareous deposits were not observed.

Vessels in the vascular stria and in the modiolus appeared to be normal in all

Table 2. Temporal Bones

Group	Organ of Corti, comments	Vessels in the internal auditory canal, including the intraneural vessels	Ganglion cells in the basal cochlear coil	The auditory nerve inside the internal auditory canal	
				Peripheral part	Glial part
I	Deformed and flattened	Thickening of walls, luminal stenosis	+ / +	+ / +	++ / ++
	Deformed and flattened	Thickening of walls, luminal stenosis	+ / +	++ / ++	+++ / +++
	Deformed and flattened	Thickening of walls, luminal stenosis	++ / ++	absent / ++	absent / ++
	Deformed and flattened	Thickening of walls, luminal stenosis	++ / ++	+ / +	+++ / +++
	Deformed and flattened	Thickening of walls, luminal stenosis	++ / ++	++ / absent	++ / absent
	Deformed and flattened	Thickening of walls, luminal stenosis	normal / normal	+ / +	absent / absent
	Left-sided hydrops	Thickening of walls, luminal stenosis	+ / +	+ / absent	++ / absent
	Deformed and flattened	Thickening of walls, luminal stenosis	++ / ++	++ / ++	absent / absent
II	Deformed and flattened	Thickening of walls, luminal stenosis	+ / absent	++ / absent	+++ / absent
	Deformed and flattened	Slight thickening of walls, luminal stenosis	+++ / +++	+ / +	++ / ++
III	Normal throughout	Thickening of walls, luminal stenosis	normal / normal	sporadic demye- linization	severe demye- linization
IV	Left-sided hydrops	Almost normal vessels	+++ / absent	+++ / only few myelin sheaths + axons	+++ / +++

Patients discussed in chapter IV.

Pathological findings in temporal bones.

patients; occasionally the walls had thickened moderately, but stenosis of the lumens was a rare occurrence. On the other hand, the walls of the vessels in the internal auditory canal as well as the walls of intraneural vessels had thickened in some cases and lumens might be constricted; it applied to all patients that the vascular changes were more pronounced than those in the vascular stria and the modiolus. The intraneural changes were most marked in the glial part of the nerves.

The number of ganglion cells was normal, or faintly reduced, in the apical and the middle coil of the spiral ganglion; degenerative changes, if any, were negligible. In the basal coil, however, symmetrical disappearance and degeneration of cells in the spiral ganglion ranged from slight to moderate.

According to patho-anatomical criteria, the acoustic nerve in the internal audi-

tory canal can be divided into two parts, one peripheral containing Schwann's cells and one central, glial part. In the peripheral part, disappearance and degeneration of myelin sheaths and axis cylinders would be of about the same order as in the basal coil of the spiral ganglion; in the glial part, disappearance of myelin sheaths and axis cylinders was of about the same order while degeneration was by far more intense. Numerous amyloid bodies were demonstrable at the junction between the two parts.

It should be noted, however, that Scarpa's vestibular ganglion as well as the vestibular nerve were sites of only few, if any, patho-anatomical lesions in all patients.

At gross inspection of the central nervous system, all brains were found to be diffusely atrophic; infarctions were demonstrable in a few of the brains. The leptomeninges were diffusely blurred.

Vessels in the circle of Willis were moderately to severely atherosclerotic. Dilatation of the ventricular system was of varying degrees.

Findings obtained by microscopy of the central auditory pathways included slight to moderate disappearance of cells in the glial part of the acoustic nerve and severe degenerative changes of myelin sheaths and axis cylinders. The walls of intraneural vessels had thickened.

Disappearance and degeneration of cells in the ventral and dorsal cochlear nuclei were symmetrical, being most marked in the latter. Exactly the same type of lesions were demonstrable in the superior olivary nucleus, in the inferior colliculus, and in the medial geniculate body.

Myelin sheaths and axis cylinders in the auditory pathways throughout the brain were swollen and unevenly calibrated.

The white matter in the cortical auditory centres displayed varying degrees of thinning out with degeneration of myelin sheaths and axis cylinders.

Focal and diffuse disappearance and degeneration of the cortical ganglion cells were in evidence; in addition, cortical malacias were manifest in three patients; in one of these (no. 1 in group I, table 1) the left transverse gyri were involved; in another (no. 2 in group I, table 1) both transverse gyri were involved, and in one patient (no. 5 in group I, table 1) the right transverse gyri were involved.

Vessels in the cerebrum, the brain stem, and in the leptomeninges were severely damaged. In addition to the atherosclerotic lesions observed by gross inspection, the arteries and veins of intermediate size were sites of perivascular fibrosis: the connective tissue in the walls had amplified. The walls of arterioles were of a thickened, homogenous appearance and the lumens were constricted, occasionally they might be totally occluded. Fibrillary thickening of the capillaries was in evidence.

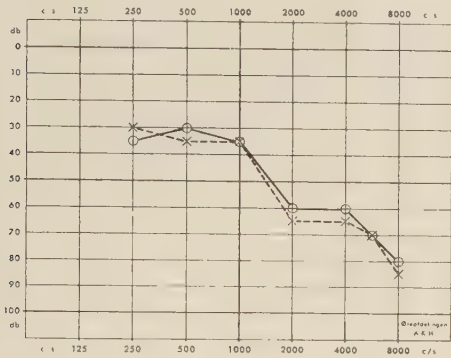
The pathological processes involving the cortex in the transverse gyri (the central auditory centres) were apparently not more severe than those in the auditory nuclei in the brain stem, whereas processes involving the glial portion of the acoustic nerve and the white matter in the auditory centres were more severe than those in the auditory pathways through the brain stem.

The processes seemed to occur symmetrically.

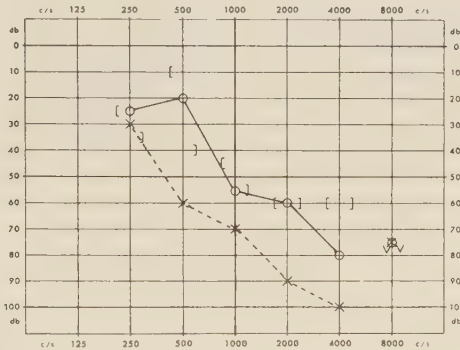
Additional sections of brains disclosed diffuse pathological processes similar to those observed in the auditory pathways.

Group II. 2 patients

The past medical histories of the two patients concerned were similar to those of patients in group I and the audiometric findings in patients in the two groups were identical (cf. fig. 6. corresponding to figs. 24–25 in treatise B).



No. 9.



No. 10.

Fig. 6. Audiogram from the patients in group II. (nos. 9–10, table 1).

In one patient (a 79-year-old man, cf. table 1), the impaired hearing may in part have been due to the noise produced by his trade since he throughout 56 years had been working as a cooper.

One of these patients died of croupous pneumonia, the other of coronary thrombosis.

Findings obtained by histological examination of the middle ear, the internal ear, and the acoustic nerve were identical with the degenerative changes observed in patients in group I, table 2.

Both brains were sites of degenerative lesions like those seen in brains from patients in group I, but atherosclerosis was not in evidence. The walls of arterioles had thickened, being of granular structure as otherwise seen in cases of senile atrophy.

Thus, findings in the ten patients in groups I and II included: symmetrical loss of perceptive hearing, pathological processes involving the temporal bones, in particular the basal cochlear coil, and degeneration of the central auditory pathways and nuclei.

Group III. 1 patient

Group III comprises only one patient whose past medical history deviates from that of the aforementioned patients in that his loss of hearing had meant a handicap since he was about 58 years old. In addition, his blood pressure, systolic as well as diastolic, was elevated.

The patient was a 60-year-old man who previously had been in good health; his hearing had been normal. During the last two years prior to death he became increasingly demented and complained of uncharacteristic vertigo and impaired hearing. One year before death, a haemorrhage in the right hemisphere occurred. Audiometry revealed symmetrical loss of perceptive hearing; the loss of hearing was of the presbycusis type and of a severity common in 75-year-old individuals, according to *Johansen's* findings in a series of normal subjects (*Johansen, 1943*), cf. fig. 7, corresponding to fig. 26 in treatise B.

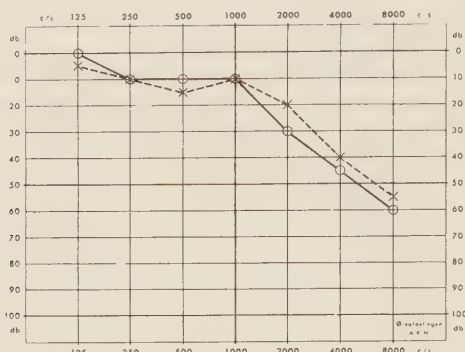


Fig. 7. Audiogram from the patient in group III (no. 11, table 1).

In addition, the loss of discrimination ranged at 67 %, determined by free-field speech audiometry.

The patient died one year later in continuation of recurring cerebral vascular episodes.

It should be emphasized that the brain was fixed *in situ* about 10 minutes after death had occurred.

Autopsy inspection of organs revealed severe, generalized atherosclerosis.

Microscopy of the temporal bones (table 2): The organ of Corti was of normal appearance. The walls of the cochlear vessels were slightly thickened. The cochlear spiral ganglion was normal.

Axis cylinders in the peripheral part of the acoustic nerve had not disappeared, but sporadic demyelination was in evidence, intensifying towards the glial part.

Vessels in the internal auditory canal and the acoustic nerves were markedly arteriosclerotic.

All lesions of the temporal bones were symmetrical.

At gross inspection and by microscopy of the brain, the right hemisphere was found to be a site of a massive, fresh haemorrhage and atrocious atherosclerosis. In the glial part of the acoustic nerve, demyelination was sporadic, intensifying towards the cerebrum where it was almost generalized. The preserved structures in the auditory pathways and centres were sites of histologically demonstrable lesions similar to those observed in patients in group I.

Group IV. 1 patient

Also group IV comprises only one patient in whom findings deviated from those observed in patients in the other groups in that audition in the left ear was extinct. Furthermore, the patient was a chronic alcoholic.

The patient was a 69-year-old man. As far as he was able to remember, hearing with his left ear had always been poor although he did not know why. Since childhood, hearing with his right ear had been fluctuating on account of periodic episodes of otitis media.

Audiometry performed six years prior to his death had disclosed that audition in his left ear was extinct; audition in the right ear could not be reliably determined (cf. fig. 8 corresponding to fig. 29 in treatise B). The patient being very shy, it proved impossible to decide whether the right-sided loss of hearing was of the sound-conduction type or of the perception type. Also speech audiometry proved a failure.

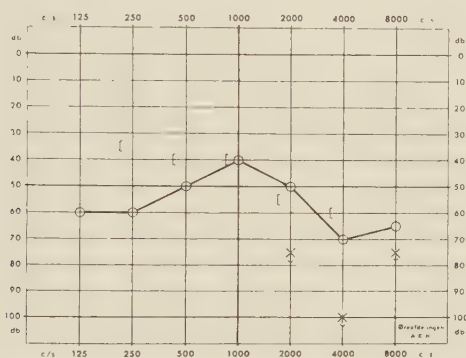


Fig. 8. Audiogram from the patient in group IV (no. 12, table 1).

The patient died when he was 69 years old, the cause of death being postoperative complications after prostatectomy.

Autopsy inspection of organs disclosed acute pyelonephritis. Arteriosclerotic changes, if any, were very mild.

By microscopy of the right temporal bone, the middle ear and the mastoid process were found to be sites of chronic, inflammatory lesions. The ossicular chain and the tympanic membrane were intact and adhesions in the middle ear were only few. Otherwise findings were similar to those observed in patients in groups I and II.

Examination of the left temporal bone displayed normal conditions in the middle ear. Nothing of the organ of Corti remained well-preserved. Labyrinthine hydrops, involving also the saccule, was manifest. Cells in the spiral ganglion had disappeared almost completely and myelin sheaths and axis cylinders were scarce in the acoustic nerve.

After fixation of the brain it weighed 1300 gram. It appeared normal to the gross view and without signs of arteriosclerosis.

Microscopy of the brain disclosed disappearance and degeneration of axis cylinders and myelin sheaths in the glial part of the acoustic nerve. On the right side, the changes were moderate, disappearance of cells being almost total on the left side where also the few remaining axons had degenerated.

The auditory nuclei throughout the brain stem were sites of moderate degenerative changes and the cerebral cortex displayed mild atrophy.

The most severe pathological lesions were localized to the white matter in the brain stem as well as to auditory centers in the cerebral hemispheres where disappearance of cells was marked and degeneration of myelin sheaths severe; similar lesions were demonstrable also in areas other than the auditory pathways.

The most significant findings, clinical as well as histological, in this patient included: audition in the left ear was extinct, audition in the right ear being severely impaired; almost total disappearance of neurones in the left spiral ganglion, and moderate degree of disappearance and degeneration of neurones in the right spiral ganglion of the cochlea. The brain was a site of diffuse demyelination.

Discussion

A brief account is given concerning data included in the past medical histories of the 12 patients comprised in this series together with descriptions of the severity of their loss of hearing and the pathological processes observed in their temporal bones and brains.

The question to arise is whether it may be possible on the basis of the obtained findings to single out such lesions of peripheral and/or central elements in the auditory pathways as may be responsible for the loss of hearing.

The most essential pathological findings in temporal bones of patients in groups I and II included:

Flattening of the organ of Corti which, in most cases, may have occurred after death. Uniform, rather moderate vascular changes throughout the cochlea. Slight to moderate disappearance of cells in the basal coil of the spiral ganglion together with degenerative lesions involving the peripheral part of the acoustic nerve, paralleling the changes of ganglion cells. All of the observed findings were symmetrical.

The pathological processes in the central auditory pathways were also symmetrical. The slight to moderate disappearance of nerve fibres and the severe degeneration of the central glial part of the acoustic nerve were more marked than the disappearance and degeneration in the peripheral Schwann part; degeneration of auditory pathways through the brain stem of the cortex was obviously most marked in the white matter of the cerebral hemispheres. Furthermore, atrophy of the cerebral cortex was manifest, being particularly marked in the two patients belonging in group II.

Flattening of the organ of Corti and of other structures in the middle scale was observed in 11 patients. According to previous publications, this feature need not be a constant finding in elderly patients with poor hearing; the phenomenon has been observed also in subjects whose hearing was normal (*Crowe et al.*,

1934; Saxén, 1952). Furthermore, the epithelial lesions may have occurred after the death of the patients and thus, they cannot have been responsible for their loss of hearing (Lange, 1937; Fleischer, 1956). The latter is corroborated by the fact that the organ of Corti was found to be normal in the patient belonging in group III as well as in the 43-year-old male patient with fluctuating audition in whom a glioblastoma developed; the patient has been discussed in chapter II. In both cases, the organs were fixed within 10 minutes after death.

Loss of perception of tones in the low-frequency range varied in these patients although the ganglion cells in the apical and middle coils seemed to be normal, or only slightly degenerated, thereby excluding that this part of the hearing loss was due to cochlear changes. The same conclusion has been drawn by Saxén (1952) on the basis of findings in his series.

The basal coil was the site of slight to moderate disappearance of ganglion cells; to a certain extent, although not completely, this feature may explain why the hearing of high tones was impaired in these patients. The lesions concerned, however, were not more severe than those which according to the available literature may be encountered in patients with normal hearing (Crowe *et al.*, 1934; Schuknecht, 1955; Citron *et al.*, 1963).

If the rather slight vascular changes in the cochlea actually had exerted an influence on the organ of Corti and on the degenerative processes in ganglion cells, degeneration might be expected to be uniform throughout all coils because the vessels were of uniform appearance throughout the cochlea.

To all appearances, the degenerative changes of the peripheral (Schwann) part of the acoustic nerve seemed to equal those of the ganglion cells pertaining to the basal coil. These changes seemed out of proportion to the very severe changes involving the extraneural vessels within the internal auditory canal.

By way of comparison it should be noted that the vestibular nerve as well as Scarpa's ganglion were normal; degeneration, if any, was of a mild degree in all patients.

In the central auditory pathways, degeneration was of a severe character in the glial part of the acoustic nerve and in the white matter in the brain stem as well as in the auditory centres in the cerebral hemispheres. The changes were more pronounced in the cerebral hemispheres than in the white matter of the brain stem.

The pathological processes in the auditory nuclei in the cortex were a little less pronounced than those involving the axons and axis cylinders in the auditory pathways.

The cerebral changes might be due either to advanced age or to impaired vascular conditions; it must be admitted, however, that the cortical atrophy diagnosed in patients in group II was appreciable.

There is reason to believe that the above discussed pathological processes involving the central nervous system in patients in groups I and II may have compromised their audition; hence, lesions involving the cerebral sections of the auditory pathway may have been responsible for the loss of hearing, in particular that applying to low tones, to a minor degree than applying to high tones.

It is rather remarkable that the cochlear structures were normal throughout in

the patient in group III, while sporadic demyelination, intensifying towards the cerebrum where it was almost generalized, was in evidence in the acoustic nerve. In this case it proved rather difficult to inspect the white matter and the cerebral cortex because of the oedematous nature of these. From a clinical point of view, however, the patient concerned was almost completely demented and hence, the pathological processes to precede the acute and fatal attack must have been of a severe degree.

This patient's loss of hearing applied almost exclusively to tones in the high-frequency range and, as the cochlea was of normal appearance, the hearing loss could hardly be attributable to cochlear factors; it may rather have been due to changes in the acoustic nerve and in the central nervous system.

Lesions involving the right cochlea and the acoustic nerve in the patient in group IV were identical with those encountered in patients in groups I and II. It should be mentioned, however, that mild, chronic, inflammatory changes involving the middle ear on the right side were manifest in the former patient. The degree of the inflammatory lesions was not more severe than that otherwise seen in patients with normal hearing (*Crowe et al.*, 1934).

The auditory pathways in the brain stem and in the cerebral hemispheres were sites of symmetrical, extremely severe pathological processes in the white matter; processes were less pronounced in the nuclei and the cortex. Arteriosclerosis was not in evidence. It seems reasonable to conclude on the basis of these findings that the right-sided loss of hearing was due mainly to cerebral changes in this patient.

Flattening of the organ of Corti in the left ear, where audition had been extinct throughout years, was more marked than that in the right ear; hydrops was manifest and the spiral ganglion as well as the acoustic nerve were almost completely eliminated. Since lesions in the central nervous system were symmetrical it seems reasonable to presume that the left-sided loss of hearing, in excess of the right-sided loss, might be ascribable to the degenerative processes in the peripheral organ.

On the basis of the findings in these 12 patients it seems justified to conclude that pathological cochlear lesions were not solely responsible for their loss of hearing, rather the pathological processes in the brain may have played some role, probably even a major role.

Hearing losses observed in these 12 patients were in some cases of the presbycusis type, but hearing curves of other configurations were also obtained.

For instance, the hearing loss experienced by the 60-year-old patient (no. 11, group III) was of the presenile type and the hearing curve obtained in that case reminded of the one seen in cases of presbycusis which, according to the available reports, may be encountered in 75-year-old subjects whose audition is "pertaining to age".

Furthermore, the loss of hearing of tones in the high-frequency range in patients nos. 6 and 7 in group I was more marked than that otherwise seen in patients whose hearing is impaired because of age; in four patients (nos. 1, 3, and 4 in group I, and no. 1 in group IV), the loss of hearing applying to the low-frequency range was also of a more severe degree than otherwise seen among patients whose hearing is impaired because of age.

In fact, it was not possible in any of the 12 patients concerned to demonstrate a correlation between the degree of the pathological processes in the internal ear and the demonstrable loss of hearing, no matter whether the hearing loss applied to tones in the high- or low-frequency range.

The conclusion to be drawn is therefore that loss of hearing "pertaining to age", presenile loss of hearing of the presbycusis type, as well as loss of hearing displaying audiometric curves of different configurations, apparently occur as sequelae of pathological processes involving the cerebrum as well as the temporal bones.

CHAPTER V

Pathological Processes Involving the Temporal Bone and the Cerebrum in a Senile Patient with Ménière's Disease

The present chapter comprises a review of the past medical history of an 83-year-old patient with Ménière's disease together with a summary of the histological findings in the temporal bones and the brain of this patient. The clinical and histological findings are collated with those obtained in similar studies of Ménière's disease as reported in the relevant literature. A more detailed account is available in treatise C.

The patient was an 83-year-old woman who always had enjoyed a good health, apart from chronic arthritis and moderate dyspeptic complaints.

At the age of 50 years, the patient had been hospitalized on account of Ménière's disease, manifesting itself as intensifying tinnitus, impaired right-sided hearing capacity, and episodes of vertigo. She managed to hear speech whispered *ad aurem* and hearing with the left ear remained normal.

Episodes of vertigo subsided, but her sensations of instability as well as the right-sided tinnitus and the ipsilaterally reduced hearing persisted.

Ten years later the episodes of vertigo recurred (any detailed data are not available). Hearing with the left ear remained uncharged and satisfactory.

At the age of 77 years, i.e. 27 years after onset of the initial symptoms, episodes of vertigo recurred frequently and hospitalization was required. Moreover, hearing with her left ear failed and all sounds seemed to be distorted. Audition tests at that time revealed: whispers r/l = aa (ad aurem)/ 0.50 meter; speaking voice r/l = aa/3-4 meter.

Vestibular irrigation disclosed a severely reduced caloric functioning of both ears. Romberg's test was positive; when the patient was walking with her eyes closed, she would constantly be deviating to the left. Episodes of vertigo subsided within a couple of weeks. A cataleptic attack occurred while she was in hospital.

At the age of 78 years the patient applied for treatment in the State Hearing Centre in Aarhus; furthermore, she wanted to have a hearing aid. Audiometry disclosed a severe bilateral deafness of the perception type, cf. fig. 9, corresponding to fig. 1 in treatise C.

Speech audiometry revealed that the left-sided threshold of intelligibility ranged at 50 db, the loss of discrimination ranging at 90 %. The patient managed to perceive sounds, but not speech, with her right ear. She complained of non-rotatory vertigo and besides, a high-pitched tone persisted in both ears. She was supplied with a hearing aid, but she had no benefit from it and returned it.

At the age of 79 years, the patient consulted an otologist because of a sore

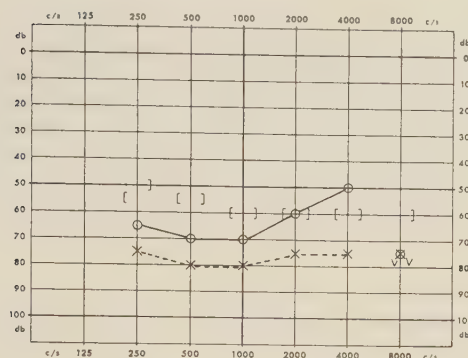


Fig. 9. Hearing curve from the senile patient with Ménière's disease.

throat, but the origin of this complaint could not be defined; an inexplicable paralysis of the right vocal cord was diagnosed.

The patient died at the age of 83 years.

Autopsy inspection of organs disclosed: "Thrombosis a. pulm sin. et infarctus lobi inf. pulm sin; pneumonia sin; and atrophica fusca et arteriosclerosis organorum m.gr."

Microscopy of the right and left temporal bones:

The cochleae were sites of bilateral labyrinthine hydrops, most severe on the right side where also the sacculus was involved. The right utricle was slightly dilated while the semicircular canals appeared to be normal. The tectorial membrane was apparently forced downwards over the organ of Corti. Some areas of Reissner's membrane were of atrophic appearance while proliferation of epithelial cells was in evidence in other areas.

In the right spiral ganglion of the cochlea, the disappearance of cells was of a rather considerable degree at the level of the basal coil, being almost negligible at levels of the middle and apical coils. An even higher degree of disappearance of cells was observed in the left spiral ganglion where it was most pronounced at the level of the basal coil.

In the peripheral part of the right and left acoustic nerves the disappearance of axons was appreciable, being almost of the same order as the disappearance of ganglion cells; remaining axons had degenerated, most markedly on the left side.

The vestibular portions of the labyrinth were of normal appearance on either side which also applied to Scarpa's vestibular ganglion and the vestibular nerve.

Gross inspection of the cerebrum:

- (1) A subdural haematoma of long standing was in evidence over the anterior portion of the right cerebral hemisphere.
- (2) Diffuse cortical atrophy.
- (3) Moderate blurring of the leptomeninges.
- (4) Atherosclerotic lesions involving the circle of Willis and extending into the peripheral ramifications.

Microscopy of the central auditory pathways:

Severe degrees of disappearance and degeneration of axons in both acoustic nerves, but most pronounced in the left. The auditory pathways and nuclei were sites of severe outfall and degeneration of ganglion cells and axons. Ganglion cells in both auditory centres had also disappeared and degenerated; the disappearance and degeneration of myelin sheaths and axis cylinders in the white matter were of a similar, severe degree.

Microscopy of the central vestibular pathways and centres:

The glial part of the vestibular nerves on both sides had degenerated. The course of nerves between the restiform body and the nucleus of the spiral tract of the trigeminal nerve could not be reliably followed. The lateral-, medial-, and superior vestibular nuclei on either side displayed excessive disappearance and severe degeneration of ganglion cells, the phenomenon being most marked on the left side.

Furthermore, severe, diffuse degeneration of nuclei and pathways throughout the brain stem was demonstrable in this patient; lesions seemed to be most pronounced in the vestibular parts of the nuclei of the cranial nerves.

Vessels in the brain stem and the cerebrum displayed signs of capillary fibrosis, arteriolosclerosis, and atherosclerosis.

Thus, in this 83-year-old patient who since the age of 50 years had been suffering from Ménière's disease and in whom an additional loss of hearing of high tones had been ascertained when she was 77 years old, findings included:

- (1) Bilateral labyrinthine hydrops.
- (2) Degeneration and disappearance of neural elements in the acoustic nerves, parallel to features in the corresponding spiral ganglion of the cochlea, and most pronounced on the left side.
- (3) A normal left Scarpa's ganglion (the one on the right side was not included in the sections), and a rather mild degree of degeneration of axons in the Schwann part of both vestibular nerves.
- (4) Disappearance and severe degeneration of structures in auditory as well as vestibular central nuclei and pathways.

Discussion

The clinical and histopathological findings in this patient shall be briefly discussed and be related to findings obtained in previous works by other investigators.

A: Lesions involving the epithelial portion of the labyrinth

(1) *Labyrinthine hydrops*

Mygind & Dederding (1938) were the first who recognized that changes in the endolymphatic pressure might be responsible for various degrees of hearing loss applying to the low-frequency range when episodes of Ménière's disease occurred;

this hypothesis has later been corroborated by experiments on models as well as in animals (Tonndorf, 1957; McCabe & Wolsk, 1961). Arslan *et al.* (1963) arranged sodium chloride crystals on the round window in man, thereby changing the pressure in the labyrinth; this procedure would be followed by a development of typical attacks of Ménière's disease in the patient concerned.

On the assumption that the intralabyrinthine hydrops was the exclusive cause of the patient's loss of hearing, audition should be expected to be reduced to a degree paralleling the degree of distension of Reissner's membrane. In the case at issue, however, audition was best preserved in the right ear in which hydrops was most severe and most widespread. Furthermore, hydrops was unilateral and involved the sacculus in one senile patient (no. 7 in group I) discussed in chapter IV; this patient did not present symptoms of Ménière's disease whereas his loss of perceptive hearing, confined to the high-frequency range, was symmetrical. Also the loss of discrimination was equal on both sides. This invalidates the theory that hydrops *per se* was solely responsible for the hearing loss applying to the low-frequency range.

Descriptions of labyrinthine hydrops associated with dilatation of the sacculus are on record (Rollin, 1940; Kristensen, 1961). In the patient here concerned, dilatation of the sacculus was of an unilateral nature while hydrops in the cochlear coils was bilateral.

(2) Injury to the organ of Corti

Pathological lesions of the organ of Corti as well as their importance for audition are not easy to evaluate. Schuknecht (1953) and Kristensen (1961) observed in their patients with severe hydrops that the pathological processes were most pronounced in the apical coil and thus, might account for the hearing loss applying to low tones. On the other hand, Lindsay & Schulthess (1958) found that the organ of Corti seemed to be fairly normal at the site of the apical coil whereas the loss of ganglion cells in the same area was rather appreciable. In patients with Ménière's disease, however, there will always be some recruitment which serves to confirm that the function of hair cells is reduced (Dix *et al.*, 1948; Hood, 1961).

In the present case it could not be reliably ascertained whether the changes in the organ of Corti were more severe than those otherwise seen in cases of presbycusis in patients of equivalent ages (chapter IV); on the contrary, sections from all coils gave evidence of a surprisingly well-preserved organ of Corti.

(3) Changes involving the remaining epithelial structures in the middle scale

According to available reports, specific changes of supporting cells in the cochlea, the vascular stria, the basilar membrane, and the tectorial membrane, have not been observed in patients with Ménière's disease and were not seen either in the present case.

(4) Changes involving the epithelial portion of the peripheral vestibular organ

Endolymphatic hydrops in the semicircular canals has never been observed in patients with Ménière's disease and the utricle is rarely involved (Hallpike &

Cairns, 1938; Rollin, 1940; Lindsay, 1960, Kristensen, 1961, 1962). Electron microscopy revealed lesions involving the superficial layers of the sensorial epithelium in the ampullae of the semicircular canals (Pietrantonio & Iurato, 1960; Litton & Lawrence, 1961). The latter authors held that the pathological changes had been in evidence prior to death and also that the process responsible for the development of Ménière's disease might bring about a cytotoxicity that was seen to persist almost until cell death; accordingly, the peripheral vestibular function would be reduced, it might even be discontinued.

It seems rather difficult, however, to explain the intensive vestibular symptoms solely as sequelae of the pathological processes in the labyrinth. Busanny-Caspari & Matzker (1960) did not observe any signs of hydrops in a lateral semicircular canal which was removed at the moment when the patient had a severe attack of Ménière's disease. Moreover, Lindsay (1960) found vestibular reactions to be normal in patients with highly advanced hydrops. Even so, Lindsay postulated that the vestibular reactions to occur during attacks are best explained on the assumption of an existence of a factor of mechanical nature which may upset the ampullary mechanism in one or more ampullae.

Apart from the moderate dilatation of the right utricle, pathological processes in the vestibular portion of the labyrinth were not in evidence in the patient here discussed.

B: Changes involving the neural elements of the labyrinth

(1) The auditory portion of the labyrinth (1st neurone of the auditory pathways)

Several authors have observed in patients with Ménière's disease that the pathological processes in ganglion cells in the apical cochlear coil paralleled the loss of hearing of tones in the low-frequency range (Rollin, 1940; Lindsay & Schulthess, 1958; Lindsay, 1960; Kristensen, 1961). Such hearing loss has been produced in cats via lesions induced to the apical cochlear coil (Schuknecht & Neff, 1952).

In the patient at issue, ganglion cells in all cochlear coils were found to be damaged, mainly those in coils of the left cochlea; the latter is commensurate with the fact that her hearing on the left ear was most severely impaired. In contrast, in the senile patients discussed in chapter IV (groups I, II, and III), the hearing impairment as well as the pathological processes were symmetrical.

Disappearance and degeneration of neural elements were also found to be most intense in the peripheral part of the left cochlear nerve where it paralleled the degree of disappearance of ganglion cells in the spiral ganglion of the cochlea.

Dandy (1937) observed usually a large arterial branch in touch with the cochlear nerve in patients with Ménière's disease. This phenomenon was not observed in our patient.

(2) The vestibular portion of the labyrinth (1st neurone of the vestibular pathways)

The incongruity between the, often severely reduced, caloric vestibular reaction and the histological findings in the vestibular portion of normal labyrinths represents

an outstanding phenomenon which has been observed previously by other investigators (e.g. *Kristensen*, 1961) as well as by the present author.

C. Changes involving the cerebral cochlear and vestibular neurones

(1) The auditory pathways and centres

A review of the relevant literature as well as the clinical data obtained (chapter IV) suggest that a loss of hearing of tones in the low-frequency range may represent the sequelae of lesions involving sites centrally to the cochlea, either in the auditory nerve or in the brain stem. *Lundborg* (1955), *Gravendeel* (1958), *Gravendeel & Plomp* (1960), and *Parker et al.*, (1962) have advanced the same hypothesis.

In the patient here discussed, changes of the ganglion cells in the 1st neurone were not sufficiently marked to represent the factor exclusively responsible for the loss of hearing, whether of tones in the low- or high-frequency range; accordingly, such hearing loss must be attributable to factors localized to central sites; considering the histological findings in the central auditory pathways, the latter seems most probable.

(2) The vestibular pathways and centres

Reports concerning histological studies of the cerebral vestibular neurones in patients with Ménière's disease are not available. Electronystagmographic curves obtained in cases of this disease have revealed, however, some features suggestive of cerebral lesions (*Aschan & Stahle*, 1957; *Montandon*, 1959; *Maspétiol et al.*, 1961). This finding has been corroborated by *Rosberg* (1960) and *Maspétiol et al.* (1962) who for instance, on the basis of clinical deliberations suggested that the vegetative and nystagmogenic centres in diencephalon might be affected in patients with Ménière's disease. Stimulation of the hypothalamus in cats has been found to change the rate of velocity of blood perfusion in the cochlea (*Morizono*, 1966). Thus inspired, it might be worthwhile to consider whether irritative disorders in the central nervous system might exert an influence on the pressure in the internal ear.

In the patient here concerned, the extremely severe lesions involving the central vestibular nuclei and pathways were by far more intense than those in the other structures of the brain stem; the latter is in contrast to the fact that the peripheral neurones remained well-preserved.

(3) Additional cerebral lesions

Several authors have observed neurological symptoms other than those pertaining to Ménière's disease, indicating a presence of cerebral lesions. According to *Crowe* (1937), the patients might become unconscious, diplopia of transient nature might occur, and occasionally, the corneal sensitivity on the same side as the audio-vestibular symptoms might be reduced. *Podvinec et al.* (1961) observed paralysis of the trigeminal nerve, associated with endolymphatic hydrops, in 9 out of 18 patients; in one patient, Bell's palsy was seen to develop coincidentally

with the primary episode of Ménière's disease. *Greiner et al.* (1954) saw one patient in whom the lesion developed along with syringomyelia.

The patient here concerned had cataleptic attacks, unilateral paresis of the vocal cord, positive Romberg's symptom, and besides, she would constantly be deviating to the left if she were walking with her eyes closed, symptoms which all may be attributable to diffuse cerebral lesions.

Furthermore, some authors have suggested that the aetiology of Ménière's disease might include cerebral vascular lesions and accordingly that "vascular crises" might be responsible for the sporadically occurring symptoms. For instance, symptoms of Ménière's disease have repeatedly been observed in patients whose complaints might be ascribable to vascular diseases such as Quincke's oedema (*Dederding*, 1929), glaucoma (*Godtfredsen*, 1949; *Hilger*, 1950), migraine (*Sørensen*, 1959), lesions of the conjunctival vessels (*Naito*, 1962), and "extensive vascular disorders exciting symptoms of transient nature in the trigeminal nerve and the facial nerve" (*Podvinec et al.*, 1961).

In the present case, the vascular changes were never seen to be of a degree more severe than that otherwise seen in senile patients like the ones discussed in chapter IV; especially not the lesions at the site of the circle of Willis.

It emerged from the review of the literature that opinions of and views on the localization, or localizations, of the pathological processes responsible for a development of Ménière's disease were highly conflicting.

On the basis of the histological findings in the patient here concerned it may be presumed that her symptoms were due to lesions at peripheral as well as central sites, mainly to those at central sites. Whether the patient's loss of hearing of high tones is to be taken as a symptom of Ménière's disease or it was due rather to her age and the severe arteriosclerosis, remains to be decided, but the pathological findings suggest that her hearing loss applying to the high-frequency range originated in lesions at peripheral and, especially, at central sites.

PART 2

Studies of Vessels in Temporal Bones after Injection of Contrast Medium

The subject matter of Part 2 is the results obtained by injection of contrast medium into vessels of human temporal bones. The primary object was to investigate whether vessels in the membranous labyrinth have to pass a capillary system before they come into communication with vessels in the surrounding osseous structures. Another object was to describe the anatomy of the vascular pattern in the cochlea and the acoustic nerve in subjects at various ages, in an attempt to defining the aetiology of the lesions discussed in Part 1.

Chapters VI, VII, VIII, and IX are abstracts of the previously published treatises D, E, F, and G; chapter X contains a summary of all findings obtained and discussed in parts 1 and 2 and the ensuing conclusions.

CHAPTER VI

Material and Methods

The material comprises 43 temporal bones from a total of 33 individuals at ages ranging between five days and 94 years.

Any selection of specimens has not been possible; the material comprises 11 temporal bones from 11 "unclaimed bodies" autopsied in the Los Angeles County Hospital, together with 32 temporal bones from 23 patients who died in Odense Amts og Bys Sygehus (the University Hospital in Odense).

The group termed "unclaimed bodies" comprises the bodies of patients who died in the Los Angeles County Hospital or had been brought into the hospital with a view to post-mortem examination and subsequent embalming. The clinical findings were not specified. According to a rough estimate based on data provided by the pathologist, ages of these subjects ranged above 50 years; the sex of patients is not on record. The author removed the first specimens, but received later temporal bones that had been removed by members of the staff trained for this purpose.

After moving to Odense, the author removed specimens from patients there. Temporal bones were obtained from 7 women and 15 men. The ages of patients were as follows: One 5-day-old boy (premature by two months); the age group 20–29 years included one man; the age group 40–49 years included two women and one man; the age group 50–59 years: two women and three men; the age group 60–69 years: one man; the age group 70–79 years: two women and four men; the age group 80–89 years: one woman and two men; finally, two men were 92 and 94 years old, respectively. Audiological and otological examinations had been performed in three of these cases; reduced hearing of the presbycousis type was diagnosed in all three.

The patients died of diseases which had not affected the temporal bones except in cases where the pathological changes were sequelae of generalized arteriosclerosis.

As regards patients who died in the Odense hospital, the bodies were transferred to the morgue about 6 hours after death and kept there at about -5° C. The patients who died in Los Angeles were also kept in the morgue, but intervals between death and transfer to the morgue might be of varying lengths.

The temporal bones were removed as soon as possible after death; in the case of bones obtained from patients in Los Angeles, they were removed about 24–48 hours after death, but prior to embalming. Temporal bones from patients who died in the Odense Hospital were removed at intervals after death ranging between 7 and 24 hours.

The temporal bones were removed and prepared in accordance with the following method, elaborated by the author (cf. treatise D):

1. The cerebral hemispheres were tilted backwards. The tentorium cerebelli was cut as close as possible to the superior petrosal sinus. The cranial nerves I–VI and the internal carotid arteries were bisected, upon which the cerebral hemispheres could be everted further backwards.
2. Prior to further dissection the anatomy of vessels and nerves in the cerebello-pontine region was studied. As to the series originating in Odense, a substance with a particle size of 0.1 micron in 1 % aqueous solution (Lichtblau 2 R "Bayer") was injected in order to facilitate identification of vessels and, if possible, to make photographic studies. The results obtained in these experiments (unpublished data) were submitted in a lecture read to the "International Course in Transtemporal Microsurgery of the Internal Auditory Canal", Zürich, March 1970.
3. The glial part of nerves VII and VIII was cut at the site of their entrance into the brain stem. Furthermore, about 3–4 cm from the medial orifice of the internal auditory canal and the subarcuate fossa, the vascular system which enters into the temporal bone from the posterior surface of the petrosal part was cut off. In order to have a sufficiently large vascular section available for the later injections, part of the cerebellum was usually included. The mass of tissue thus produced was cautiously covered by gauze which served as protection during removal of the temporal bones.
4. Care was taken to spare the temporal bone squama while the petrosal part, portions of the mastoid process, the middle ear, and the medial portion of the external auditory canal were removed. The damage thus inflicted to the base of the skull was trifling and both temporal bones could be excised.
5. The specimens were immersed in physiological saline and taken to the laboratory where they, either immediately or after storage in the refrigerator at about -4°C for some days, were kept in a specific holder designed by the author and built by Jack Urban, Urban Engineering Co., Burbank, California. It is an advantage of this holder that it permits dissection from all angles (cf. fig. 2, treatise D); moreover, fitting of a small platform makes it possible to keep the aforementioned mass of vessels and nerves level with the medial orifice of the internal auditory canal. Fitting of another specially designed equipment for vascular injections permitted delicate manipulation and sufficient stability.
6. A surgical microscope was used while a syringe was inserted into the vessel or vessels into which injections were applied. All other vessels were compressed by "micro-bulldog" clamps. Subsequently the injections could be applied without wasting much of the contrast medium.

According to the experience gained by the author, the time interval between death and removal of temporal bones, as well as the interval between removal of bones and injection of contrast medium, were of no significance for the results to be obtained.

Vessels were traced in accordance with the following techniques:

- a. Injection of "Microphil" (Canton-Bio-Medical Products, Canton, Mass.).
- b. Injection of suspensions of various porcelain dyes, namely sulphides containing circular grains of sizes ranging between 0.5 and 1 micron in 10 % gelatine. The suspensions were prepared by the author.
- c. Histochemical demonstration of the alkaline phosphatases of vascular walls, thereby reproducing the vessels in a distinct, reddish-violet contrasting colour. Initially the enzyme in the vascular walls had been fixed by injection throughout 30 minutes into the specimen, using buffered (pH about 7) formalin calcium (1 % CaCl_2 in 4 % formaldehyde) at room temperature, immediately followed by continued injection throughout 30 minutes of about 10 ml of Burstone's azo-solution for the staining of alkaline phosphatases.

The solution was prepared as follows:

- (a) Naphthol-As-Bi phosphoric acid (Sigma Chemical Company) 4–5 mg dissolved in 0.25 ml of N, N-dimethyl formamide.
- (b) addition of 5 ml of distilled water.
- (c) addition of 5 ml of 0.2 mol Tris buffer (pH 8.3–9.0).
- (d) addition of 30 mg of Red Violet LB in the form of diazonium salt followed by vigorous shaking of the mixture.
- (e) the incubation medium was filtered and immediately injected into the specimen.

The result appeared in the form of a reaction product of a reddish-violet colour.

Since the reddish-violet colour might be rather close to the blueish-violet colour which at the subsequent microscopy of the specimens was seen to develop as an optic error, a solution comprising exclusively formol calcium, but no subsequent injection of azo-dye, was injected into one control specimen (not included among the above mentioned 43 specimens).

All of these solutions (a, b, and c) were preferably injected under physiological pressure, oscillating between systolic and diastolic rates of pressure; injections into temporal bones from unclaimed bodies were applied at pressures ranging around 150 mm/mercury, owing to the lack of data concerning these patients.

In the case of solutions of type "a", processes of injection covered 15 minutes, covering 30 minutes in the cases of types "b" and "c".

In some temporal bones, differently coloured contrast media were injected into various vessels in order to demonstrate vascular anastomoses, if any, between the individual vascular systems into which injections had been applied. In order to demonstrate whether anastomoses between the basilar artery and branches of the carotid artery were in evidence, a dye material was injected into seven temporal bones via branches of each of the two arterial systems. Injection into branches of the carotid system was performed in the autopsy room after the common carotid artery had been clamped at the site inferior to the site of injection; the internal carotid artery was clamped at an intracranial site close to the cavernous

sinus. In addition, the superior thyroid artery, the lingual artery, and the external maxillary artery were compressed. Great quantities of the contrast medium were wasted during this process and the pressure could be maintained only at a level which, on an estimate, ranged below 100 mm/mercury; injections were applied over time intervals covering about 2 minutes. During injection, the anterior and the posterior surfaces of the petrosal part of the temporal bones were observed. When injections had been in progress for a few seconds, the contrast medium would appear below the dura mater in the area surrounding the geniculate ganglion. Injections were not discontinued until dural vessels in the posterior surfaces, probably also the subarcuate artery, had been filled via structures in the temporal bone. Two of the temporal bones were left without a second injection via branches of the basilar artery; they were to serve as controls.

The entire material has been classified according to the vessel or vessels into which injections were applied as well as according to type of medium used for the injections.

	Nos. of specimens
I. Injection via a.i.c.a. (anterior inferior cerebellar artery), Microphil	28
II. Injection via a.i.c.a., 10% gelatine suspension	2
III. Injection via a.i.c.a., alkaline phosphatase reagent	1
IV. Injection via the common carotid artery exclusively, Microphil	1
V. Same as item IV except that a 10% gelatine suspension was used	1
VI. 2 injections: (1) 10% gelatine suspension into the common carotid artery; (2) Microphil via a.i.c.a.	1
VII. 2 injections: (1) Microphil via the common carotid artery; (2) Microphil via a.i.c.a.	3
VIII. 2 injections: (1) Microphil via the carotid artery; (2) alkaline phosphatase reagent via a.i.c.a.	3
IX. 2 injections of Microphil: (1) via the subarcuate artery; (2) via the internal auditory artery	2
X. 2 injections: (1) Microphil via a.i.c.a.; (2) Microphil via the inferior petrosal sinus	1
In total:	43

7. After injection of contrast medium, the specimen concerned was immersed into a 3.7 % solution of formaldehyde buffered with marble. All specimens except those to which alkaline phosphatase reagent had been applied were thoroughly perfused throughout 30 minutes with an 0.5 % solution of osmic acid applied via an orifice in the superior semicircular canal and the round window. As a result of this process, the epithelial structures of the labyrinth and the mucous membrane of the middle ear would be stained a brownish-black colour that contrasted the injected dye materials.

Specimens into which Microphil and/or 10 % gelatine suspensions had been injected were prepared as follows:

8. Decalcification by an 0.7 M solution of the tetrasodium salt of EDTA, pH 7.4, at 37°. Decalcification was discontinued as soon as X-ray control had showed that all calcium was eliminated, usually after decalcification for 2 or 3 months.
9. Dehydration in rising concentrations of ethyl alcohol (25 %–50 %–70 %–96 % absolute alcohol) over a period of one week.
10. Embedding in celloidine at room temperature (2 %–6 %–12 %), usually throughout 2 or 3 months, followed by hardening in 70 % ethyl alcohol for one week.
11. Mounting of specimens onto cutting blocks by means of 10 % celloidine, followed by hardening in 70 % ethyl alcohol, lasted for about 1 week; subsequently the blocks were cut into sections of a thickness ranging from 500 up to 800 micron. The sections tolerated storage for an unlimited time until the further processes were to be performed.
12. The celloidine was removed by equal portions of ether and absolute alcohol; two treatments in this fluid were generally used, each covering 2 or 3 hours.
13. Clearance of sections in methyl salicylate.
14. With a view to a further cutting of these thick sections into thinner ones (cf. procedure described in treatise G), the aforementioned embedding in celloidine was repeated and the blocks were cut into sections measuring 7 micron.
15. Additional staining by routine histochemical methods such as haematoxylin combined with periodic-acid-Schiff (PAS) or toluidine blue.

Specimens in which vessels had been reproduced by staining of the vascular walls *per se*, using alkaline phosphatase reagents, were further dissected as follows:

- a. The bone was removed by a diamond drill until nothing but a shell of bone, measuring a few millimeters across, surrounded the membranous labyrinth.
- b. Subsequent decalcification with R.D.O. (Trade Mark Bethlehem Steel Corp.) for 10 hours at room temperature.
- c. Cutting on the freeze-microtome into sections measuring 25–30 micron.
- d. Embedding in gelatine jelly.

As regards the preparation of the thick, cleared sections, the above technique has been used previously by other investigators, for instance, *Eichler* (1910), *Levin, N. A.* (1964), and *Levin, V. N.* (1969).

Note: Application of this technique was suggested to the author by Dr. William House, M.D., Los Angeles, who also supported the decalcification project by means of a grant placed at disposal at the meeting of the Otological Medical Foundation in July 1967. Specimens were forwarded to the University Clinic in Odense where the author supplemented the series with specimens into which more than one dye material had been injected.

Note: The vascular nomenclature used in the ensuing chapters is the one introduced by *Axelsson* (1968).

CHAPTER VII

Vascular Anastomoses Between the Membraneous Labyrinth and the Surrounding Structures

Vessels in the membraneous labyrinth of the temporal bone have hitherto been considered end-arteries which, by an endosteal capsule, seem to be cut off from vessels in the surrounding bone (*Seymour*, 1954; *Arslan*, 1963; *Anson et al.*, 1966). By now, however, it is generally agreed that numerous vessels communicate with the surrounding tissues during foetal life and throughout the first two or three years of life, namely before the endosteal layer has fully developed (*Zange*, 1919; *Bast*, 1942; *Levin*, 1964; and *Anson et al.*, 1966).

As to the viability, and thus the vascularization, of the endosteal layer *per se*, some doubt is still prevailing. For instance, *Rius and Mendoza* (1961) and *Sërser and Krmpotić* (1966) declared that this layer was non-viable while *Rüedi* (1963) held that the endosteal layer was supplied from a branch of the auditory artery. *Zechner and Altmann* (1969) agreed with the latter in that the said layer was vascularized, although poorly. *Gussen* (1968) found that it might be an expression of a certain viability that the tissue lining the endosteal layer facing the membraneous labyrinth contained mesenchymal cells, including osteogenic as well as chondrogenic properties, which feature might be encountered even in aged individuals.

Several authors have discussed the defects which throughout life may involve certain areas of the endosteal layer. Such defects might provide a possible intercommunication between the membraneous labyrinth and the intermediate, more richly vascularized enchondral layer of the otic capsule. These authors attached special interest to the latter sites because they might allow invasion of inflammatory processes into the membraneous labyrinth (*Politzer*, 1876; *Siebenmann*, 1894; *Eichler*, 1910; *Zange*, 1919; *Eckert-Möbius*, 1926; *Meyer*, 1933).

In the cochlear portion of the labyrinth it is mainly a matter of bone structures which, throughout the length of one coil, seem to be inserted like a coarse-meshed osseous shelf between the basal and the middle coils, thereby connecting modiolus with the enchondral layer of the otic capsule. One of the first processes of ossification to develop during foetal life originate from areas at the site of the basal portion of this bone-shelf (*Bast and Anson*, 1949). The separation between the tympanic scale and the vestibular scale is initiated at this site of ossification. As previously mentioned, the bone structure in the basal coil of this osseous separation is rather loose, in contrast to that at more apical sites, the structure of which is dense. Basally the shelf is seen to widen until it joins with the bone area which, antero-posteriorly, separates the cochlea and the vestibulum while it medio-later-

ally separates the inferior portion of the fundus in the internal auditory canal from the middle ear.

Some authors have demonstrated the presence of vascular anastomoses between intra- and extra-labyrinthine structures. For instance, anastomoses between the promontorium and the internal ear could be followed in specimens stained with osmic acid (*Politzer*, 1876) and also by a study of serial histological sections (*Siebenmann*, 1894). *Zange* (1919) and *Hansen* (1967) managed to trace a few vessels which via the bone separating the basal and middle cochlear coils connected the promontorium of the middle ear with the modiolus of the inner ear. Finally, *Bötner and Pivotti* (1954) and *Morujo* (1967) described anastomoses to the otic capsule via branches of the internal auditory artery; localizations of such anastomoses were not further specified.

In patients with otosclerotic foci involving the endosteal layer of the cochlear capsule, for instance, *Altmann* (1962) observed that such foci might invade the septa which separate the cochlear coils. It was emphasized in particular that the blood supply to the cochlea might be compromised if these foci penetrated into the bones separating the basal and the middle coils. *Rüedi* (1968) demonstrated the presence of venous anastomoses between otosclerotic foci and the membranous labyrinth, in particular at the site of the basal coil. *Kelemen and Linthicum jr.* (1969) declared that hearing loss of the perception type would occur in patients in whom the basal cochlear coil, maybe also several other coils, were infiltrated by otosclerotic foci.

According to reports available in the literature, it seems as if infiltration by otosclerotic foci via the otic capsule, or via the bony shelf separating the basal and middle coils, might be responsible for a reduced cochlear function. It is also apparent from the cited literature that the bone structure of the basal coil, particularly the structure separating the basal and middle coils, occupies an exceptional position, whether considered from embryological, bone-morphological, vascular-morphological, histopathological, or functional points of view.

Within the cochlear modiolus, the basal portion, i.e. the portion facing the osseous shelf by which the basal and the middle coils are separated, seems to be vascularized to a higher degree than those at more apical sites. At the former site, the cochlea is supplied mainly by the spiral modiolar artery as well as by the cochlear branch of the vestibulo-cochlear artery whereas vascularization at apical sites, via the spiral modiolar artery, is less abundant (*Axelsson*, 1968). This anatomical feature intensifies further the impression that the cochlear function seems to be mainly dependent on the vascular supply to the basal coil.

Some reports have been concerned with a description of areas in the vestibular part of the labyrinth where the endosteal layer either may be absent or be very thin, thereby opening up possibilities of an anastomosing between the membranous labyrinth and the enchondral layer of the labyrinthine capsule. *Siebenmann* (1894) observed areas of this type at the non-ampullary end of the three semicircular canals. According to *Werner* (1931), such defective areas might develop during foetal life as a result of resorption and destruction of the convex portion of the semicircular canals during growth of the latter. In agreement with this, *Bast*

(1942) observed the occurrence of such resorption peripherally in the semicircular canals.

Several authors, for instance *Manasse* (1905) and *Zange* (1919), observed a strand of connective tissue between the ampullae of the posterior semicircular canal and the tympanic recess close to the round window. Indeed, this might be another site through which inflammatory processes might have access and where vascular anastomoses between the membranous labyrinth and its surroundings could be found.

Author's experiments and results

The results obtained have been described and discussed as follows in treatise E:

A. Anastomosis directly uniting the membranous cochlea and the enchondral layer

Among the 40 bones which were cut into sections of a thickness ranging between 500 and 800 micron, 31 presented anastomoses of arteriolar calibre via the osseous shelf by which the basal cochlear coil is separated from the middle coil, namely anastomoses between modiolus and the enchondral layer of the otic capsule.

In all 31 cases, the injected medium was seen to penetrate to this level, or further apically, in the cochlea. In the remaining nine specimens, injection was very sparse and the injected dye material failed to reach into the said area of the cochlear capsule.

The above mentioned anastomosing vessels into which injections were applied were arteries as well as veins which individually intercommunicated with the capillary plexus surrounding the cochlear spiral ganglion. The anastomoses emerged either directly from the spiral modiolar artery or they communicated directly with the two large spiral veins; at other sites, however, a middle piece might be inserted. Such a middle piece could be seen to unite with arterioles to the basilar membrane structures, radiating arterioles to the vascular stria, and furthermore, anastomosing vessels of arteriolar calibre which emerged directly into the enchondral layer of the osseous capsule. Arterio-venous intercommunications were also demonstrable in the modiolus at the base of the aforementioned anastomoses between modiolus and the otic capsule. Thus, the pattern by which the vascular system united the modiolus with the enchondral layer appeared to be highly polymorphous. In each specimen, the number of vascular anastomoses of arteriolar calibre ranged, roughly, between five and ten; the number of vessels into which contrast medium was injected and that of identifiable vessels stained by osmic acid have been added.

The following features emerged from a more detailed analysis of the modiolar vascular system axially to the ingress or egress of the osseous anastomoses, including the capillary plexus surrounding the cochlear spiral ganglion: At basal sites of the modiolus, afflux and efflux progressed via the following groups of vessels: the spiral modiolar artery, the cochlear branch of the vestibulo-cochlear

artery, the direct extensions of the intraneural vessels of the cochlear nerve, as well as via the osseous branches through which the osseous bridge between the basal and middle coils communicated with vessels in the enchondral layer of the otic capsule. Thus arterial connection with at least four different vascular areas was demonstrable, whereas the capillary system pertaining to the neural elements of the middle and apical coils presented only two affluxes and effluxes in the capillary system facing the neural elements of the middle and apical coils, namely via the spiral modiolar artery and the intraneural vessels in the acoustic nerve.

Vessels in the basilar membrane were also found to be well-filled, especially within the basal coil. It was rather remarkable that vessels in the basilar membrane were filled even in areas where disappearance and degeneration of internal and external hair cells in the organ of Corti, reproduced by means of osmic acid, were of severe degree. The feature was in evidence for instance in the temporal bones from old patients with presbycusis.

Owing to the fact that degrees of filling differed greatly from specimen to specimen and that the relative filling might differ in medial cochlear structures (modiolus and basilar membrane) and lateral cochlear structures (vascular stria), it proved impossible to draw any conclusions concerning the distribution of passable vessels in structures of the middle scale in patients of different ages. On the other hand, numerous parallel capillary anastomoses between the vascular stria and the basilar membrane, by way of Reissner's membrane, were in evidence in a temporal bone from an about 90-year-old patient; a yellow dye material, grain size about 0.5 micron, suspended in gelatine solution had been injected into the bone via the common carotid artery (cf. fig. 6 in treatise E.).

B. Anastomosis, via the endosteal layer, between the membraneous cochlea and the otic capsule

The vascular anastomoses were found to be of two types (and two calibres), one in the form of osseous branches of calibres approximating those of arterioles and originating either from radiating arterioles of the vestibular scale or communicating with the collecting venules of the tympanic scale, the other in the form of nutritional canals or capillaries of especially small calibres, interspersed in the dense network of osseous lamellae in the endosteal layer.

These "rami ossiculorum arteriolae rectae" were demonstrable in 15 specimens. Each specimen contained only few (1-3) which all were of the same calibre as the radiating arterioles from which they emerged. They might emerge from any site throughout the course of the latter, even from sites at which they joined with the capillary system of the vascular stria. The anastomoses were evenly distributed over the cochlear coils.

In 14 bones, the injected medium had penetrated into spaces (calibres less than 1 micron) between the web-like system of osseous lamellae in the endosteal layer. Mostly it was seen at the level of the apical and the middle coils. In some specimens, the dye material had penetrated via the long and tortuous pathway

traversing the endosteal layer, finally combining with the vascular system of the enchondral layer.

In bones in which the medium had been injected via carotid arteries, it could be traced to the endosteal layer which was entered from external aspects; thence it would progress further into structures of the membranous labyrinth, a feature to be discussed in greater detail in the following chapter.

C. Anastomosis between the membranous labyrinth and the osseous capsule in the vestibular portion of the labyrinth

In 16 of the temporal bones into which medium had been injected, such direct vascular intercommunication was demonstrable in the non-ampullary part of the superior semicircular canal where the endosteal layer either was very thin or non-existent. In the lateral semicircular canal, however, this type of anastomosis was observed only in one specimen.

In five specimens, the dye material had penetrated into the fibrous strands by which the ampullae of the posterior semicircular canal communicate with the tympanic cavity.

As mentioned in chapter VI, injections of grained dye materials were in all cases followed by perfusion of the labyrinth via an orifice in the superior semicircular canal or via the round window (perfusion with 0.5 % osmic acid for 30 minutes). The osmic acid had reproduced the said anastomoses to an extent by far greater than that otherwise obtainable by injection of grained dye-material.

It should be stressed that the degree of filling to be obtained in these vascular areas was independent of the age of the individuals from whom the specimens were obtained.

Discussion and conclusion

In specimens where the contrast medium had penetrated to the loosely built bridge separating the basal and the middle cochlear coils, anastomoses of arteriolar calibres were in all cases found to communicate directly with the enchondral layer of the otic capsule. Moreover, throughout the cochlear coils, vessels of arteriolar calibre emerged from the radiating arterioles of the vestibular scale or they anastomosed with the collecting venule of the tympanic scale; hence, the vascular system in the cochlea cannot be considered composed of end-arteries.

The fact that the basal cochlear coil is the site at which anastomosing is most readily established is in further support of the findings by *Axelsson* (1968) who observed that the vascular supply to the modiolus is more abundant in the basal than in the more apical coils.

These anatomical features can be related to those encountered in experiments on guinea pigs in which the consumption of energy in the individual cochlear coils was estimated. In experiments of this type, *Meyer zum Gottesberge and collaborators* (1965) and *Rauch* (1967) found the rate of metabolism to be highest in the basal coil, gradually decreasing towards the apical coil.

While supplies of blood are most abundant and rates of metabolism highest in the basal cochlear coil, the structures at this site apparently are the ones most sensitive to circulatory disturbances as compared with structures of the more apical coils. This feature has been observed in experiments on guinea pigs exposed to venous obstruction (*Kimura and Perlman, 1956*), coagulation of the anterior inferior cerebellar artery (*Kimura and Perlman, 1958*), and obstruction for 30 minutes of the above mentioned arteries and subsequent re-establishment of the circulation (*Perlman, Kimura and Fernandez, 1959*).

Whether the observed vascular anastomoses between structures of the membranous labyrinth and the otic capsule may be of value for the preservation of the integrity of the membranous structures cannot be judged until it has been defined in greater detail how these anastomoses come into communication with vessels outside the otic capsule, for instance, vessels originating from the carotid arteries. The results obtained in studies of these vascular communications are submitted and discussed in chapter VIII.

CHAPTER VIII

Vascular Anastomoses Within Osseous Structures of the Temporal Bone

In this chapter it is attempted to illustrate the various problems involved in the anatomy, normal as well as pathological, of the otic capsule, with special regard to the further course through the latter of the established vascular anastomoses to the membranous labyrinth (cf. chapter VII).

The following topics shall be discussed:

- A. Is vascularization particularly rich in some areas of the otic capsule?
- B. Is it possible to demonstrate anastomoses between the extra- and intra-cranial vessels which supply the otic capsule? Between individual branches emerging from larger vessels from which branches extend to the temporal bone? Between arteries in the bone substance and the venous sinuses?
- C. Are the membranous labyrinth, the more remotely situated structures of the temporal bone, and the extra-cranial vessels in vascular communication via the vascular system in the otic capsule?

These topics have, according to the available literature, been discussed on few occasions only and discussions have mainly been concerned with the pathways which inflammatory processes might follow in their course through the otic capsule (Politzer, 1876; Siebenmann, 1894; Zange, 1919; Eckert-Möbius, 1926; Meyer, 1933; Wullstein, 1948; and Bast and Anson, 1949).

Re item A:

On the basis of a compendium including a review of previously published studies, as well as on the basis of personal studies, Eckert-Möbius (1926), and later also Bast and Anson (1949), demonstrated how a richly vascularized connective tissue invades the primitive cartilage of the temporal bone during foetal life. Eckert-Möbius paid particular attention to two areas, namely one surrounding the semi-circular canals (supplied by branches from the subarcuate artery), the other comprising vessels the course of which extended from the complex of the internal auditory artery to the osseous zone separating the cochlea from the vestibulum, in the antero-posterior direction, and the internal auditory canal from the promontorium of the middle ear, in the medio-lateral direction. In the early literature, this zone was termed "Cozzolino's zone"; according to Eckert-Möbius it is particularly rich in vessels and connective tissue, even at late stages during life.

Re item B:

Nager (1954) described the vascular communication between the subarcuate artery and the vascular system of the middle ear; the latter system is considered to belong to the carotid system.

Using arteriographic techniques, Djupesland (1970) managed, in one patient, to trace vessels from the basilar arterial system, via the osseous substance of the temporal bone, to the vascular system in the neck.

Re item C:

According to some authors, the course of vessels could be traced from the membranous cochlea to the middle ear promontorium (Politzer, 1876; Siebenmann, 1894; and Zange, 1919). Such anastomoses, however, are apparently rare.

In a preliminary report on the results obtained by micro-injections into the vascular structures of the temporal bone, Hansen (1967) described a technique to be used for dissection; the technique included the drilling away of osseous structures immersed into 70 % ethyl alcohol, using a stand which produced a certain transillumination of the specimen; thus, vessels into which injections had been applied could be seen to extend from the promontorium directly to structures of the basal cochlear coil. The author did not find the technique sufficient to be used for a systematic analysis of the vascular pattern in larger numbers of temporal bones and therefore preferred the conventional histological method, as mentioned in chapter VI (Material and Methods).

The results obtained have been discussed in greater detail in treatise F.

Author's studies and results

The series of 43 temporal bones is identical with the series discussed in chapter VII (Vascular anastomoses between the membranous labyrinth and surrounding structures). As previously mentioned, all bones were studied consecutively, irrespective of degrees of vascular filling. In addition to the morphological data thus obtained concerning the pattern of injections into vessels, it was possible also to decide whether contrast medium penetrated into some areas of bone more readily than into others.

In an attempt to demonstrate vascular intercommunication between extra- and intra-cranial vessels, between various branches from large vessels known to supply the temporal bone, and between arteries and veins, differently coloured contrast media were injected into one and the same bone via different vessels. At the same time it was possible to determine whether cochlea is supplied via extra-cranial vessels as well as via intra-cranial vessels.

Re item A:

In table 3, a parallel is drawn between the degree of filling in one of the areas which according to Eckert-Möbius (1926) is particularly rich in vessels, namely

the “Cozzolino zone”, and the degree of filling throughout the remaining part of the otic capsule. The table is identical with table 1 in treatise F. The term “vascular key area” has substituted that of “Cozzolino’s zone” because the vascular supply in this area is known to be particularly rich; in the present study it includes the osseous separation between the basal and middle coils; in other words, the area in which anastomoses between the cochlea and the otic capsule were found to be most abundant (chapter VII).

Table 3

		Degree of filling within the vascular key area as compared with filling in other parts of the capsule			Total
		Optimum	Equal	Poor	
Degree of filling in a.i.c.a. (*) branches	Via internal auditory artery: optimum	13	5	0	18
	Via subarcuate artery: optimum	1	not filled 3	2	6
	Degree of filling: equal	4	5	0	9
Injections into branches of the carotid artery exclusively		1	1	0	2
Two injections: (1) via the carotid artery; (2) via branches of a.i.c.a. (*)		4	0	0	4
Total		23	14	2	39

(*) anterior inferior cerebellar artery.

The degree of filling within the various areas of the otic capsule.

Among the temporal bones, those derived from old patients were found to be best filled, even though the latter might have been suffering from generalized arterio-sclerosis. Thus, in the present series, the degree of filling of vessels in the otic capsule seemed to be independent of the age of the individuals.

In excess of the “vascular key area”, the area surrounding the vestibular semicircular canals appeared to be especially well-filled; the latter applies in particular to specimens filled via the subarcuate artery.

Hence, certain areas of the otic capsule were found to be particularly easy to fill by injection of contrast medium.

Re item B:

In 13 well-filled specimens into which one dye material had been injected via the anterior inferior cerebellar artery, vessels could be traced throughout their course from the subarcuate artery to the promontory of the middle ear. In these specimens

it was possible also to follow, via the bone substance, the course of vessels from the subarcuate artery and from branches of the internal auditory artery right to the carotid canal. Calibres of these vascular anastomoses were similar to those of arterioles. Furthermore, injections directly into carotid branches made it possible to trace vessels, the courses and calibres of which parallel the former, although injections had been applied via the opposite end.

Two dye materials were injected into each of seven specimens, the first being injected via carotid branches, the other via branches of the anterior inferior cerebellar artery (Groups VI, VII, and VIII in chapter VI); the differently coloured media in all cases were found to coincide in vascular lumina the calibres of which were estimated to parallel those of arterioles. This phenomenon is most frequently encountered in the enchondral layer of the otic capsule, but indeed, contrast media appeared also in vessels of the endosteal layer as well as in those in the periosteal layer. The dye materials are traceable from one vascular area to another, even though passage through the capillary system is escaped.

Vascular anastomoses of this type were demonstrable in temporal bones from patients in all age groups.

In two specimens, dye materials of different colours had been separately injected, one via the subarcuate artery, the other via branches of the internal auditory artery (group IX, chapter VI); the dye materials were seen to penetrate into one and the same vascular segment, still escaping passage through the capillary system.

Furthermore, if a dye material of one colour was injected into basilar artery vessels in one specimen already removed from the body, and a dye material of a different colour later was injected into the inferior petrosal sinus, arterio-venous shunts of arteriolar calibre would be observed (group X, chapter VI).

Thus, experimental vascular injections of this type made it possible to obtain an impression of a profuse vascular system in which flow between extra- and intracranial vessels was unobstructed; the same applies to flows between arteries and venous sinuses in the petrosal part, namely via anastomoses of arteriolar calibre.

Re item C:

Since the above mentioned vascular plexus in the otic capsule apparently is well suited for injections to be applied to temporal bones from patients in all age groups, it was possible to demonstrate a vascular intercommunication between intralabyrinthine vessels and vessels in the otic capsule, even further to the lumen in the carotid canal and the vascular system of the promontory of the middle ear, in analogy with features described in chapter VII.

The latter type of anastomosis could be followed in 16 specimens, all of which were well-filled with contrast media. In five of these specimens, one single, thick, cleared section proved sufficient for the tracing of the vascular anastomoses from the basal cochlear coil, via the "vascular key area", to the vascular network of the promontorium. Besides, in one of these specimens, vessels emerging from radiating arterioles and extending directly to the vascular system of the middle ear were also demonstrable; in other words, anastomosing vessels can be traced

from the membranous cochlea to the middle ear via two or three layers of the otic capsule (namely: the endosteal layer, the enchondral layer, and the periosteal layer). As to the last mentioned, the periosteal layer, the course of vessels through this could be seen to proceed via the so-called "periosteal pins", i.e. vessels running perpendicular to the surface of the promontory of the middle ear until they join the vascular system in the enchondral layer. .

In two specimens into which differently coloured dye materials were applied into extra- as well as intra-cranial vessels (one specimen from group VI and one from group VII, chapter VI), contrast media of either colour were found to appear in all layers of the otic capsule as well as in all cochlear structures, including the modiolus, the basilar membrane, and the lateral membranous cochlear structures; the same applies to all cochlear coils. In addition, the contrast medium injected via the carotid artery was found to invade the vascular system of the membranous labyrinth via the otic capsule, most profusely via the "vascular key area". The same phenomenon was encountered in two control specimens into which the media had been injected exclusively via the common carotid artery (groups IV and V, chapter VI).

Discussion and conclusion

In excess of the anastomoses in the otic capsule and those between the otic capsule and the membranous labyrinth, demonstrated by means of injections using granular media or alkaline phosphatase reagents, numerous other vessels of these types were visualized by means of staining with osmic acid.

In perfectly filled specimens, even in some originating from old patients suffering from generalized arteriosclerosis, the vascular capacity via vessels in the internal auditory canal, seemed equal to that of all demonstrable anastomoses between the cochlea, directly through the various layers of the otic capsule, and into remote vascular areas. Hence, the demonstrable vascular supply via the otic capsule is apparently of value for the cochlear nutrition, it may even be of value for its structural integrity whenever the blood supply to cochleae via vessels through the internal auditory canal is compromised.

The vascularity *per se* in the osseous substance of the otic capsule has been an object of discussion in the literature.

According to some authors, e.g. *Rius and Mendoza* (1961), *Sërçer and Krmpo-tić* (1966), and *Mendoza and Rius* (1967), this vascularization was rather poor, even insufficient, and might be responsible for a development of necrotic bone processes to be encountered in all patients, no matter their age.

Against this argues the fact that *Gussen* (1968), by means of celloidine sections and conventional staining methods, found the otic capsule to be a site of a vivid bone construction and decomposition throughout life. The latter finding has been verified by *Zechner and Altmann* (1969) who studied the enzymatic activity of the same structures in temporal bones from patients in different age groups. They observed that concentrations of acid mucopolysaccharides were almost identical

in temporal bones from senile patients and in bones from much younger individuals. These authors held also that the rate of metabolism in bone structures in temporal bones ranged at a level higher than that in any other bone in the body.

The ratio of blood volumes in the otic capsule to volumes in the membranous labyrinth was studied in guinea pigs by *Morizono* (1968). Radioactive chrome (Cr^{51}) served as tracer. Accordingly, 85 % of the blood volume in temporal bones was found to be localized to the osseous capsule while no more than 15 % was localized to intralabyrinthine sites.

Many of the previously published experiments as well as the results obtained by the author of these presents, seem to indicate that the otic capsule is composed of bone which is particularly well-provided with vessels and in which the rate of metabolism is high, even in very old patients.

The conclusion to be drawn is therefore that possibilities of additional and considerable vascular supplies to the membranous parts of the labyrinth, via the otic capsule, are in evidence in all individuals, no matter their age.

CHAPTER IX

The Vascular Supply in Various Parts of the Cochlear Nerve

The cochlear nerve, like other nerves, consists of a Schwann part and a glial part.

Němček et al. (1969) have reviewed the relevant literature on the histological, histochemical, and ultrastructural appearance of the cranial nerves. In addition, they have submitted the results obtained in studies focused mainly on the "transitional zone", i.e. a narrow zone of the glial part of the nerve, adjacent to the Schwann part. This monograph shall be briefly outlined.

The nerve was found to be thickest peripherally in the Schwann part in which the supporting cells are Schwann's cells and vascularization is strikingly more abundant than in the glial part.

The glial part of the nerve consists of two parts, namely the so-called "transitional zone" and a more centrally situated glial zone. Supporting cells in the transitional zone represent a variation of the oligodendroglial cells in the central nervous system; they are of the so-called Hortega IV type, the external shape of which may remind of that of Schwann's cells, their internal structure being identical with that of oligodendroglial cells. Accordingly, these cells are termed "schwannoid cells". The rate of metabolism in the transitional zone is higher than rates otherwise observed in the nerve; not infrequently it has been considered an element in the so-called "glial barrier" surrounding the central nervous system. The supporting cells at more central sites of the glial nerve are oligodendroglial cells; as regards their structure, it does not deviate much from that of supporting cells otherwise encountered in the white matter of the central nervous system.

Takahashi (1966) compared the degenerative changes in the Schwann part of a cranial nerve (the vagus nerve) with changes in identical parts of nerves in the sympathetic nervous system and in one nerve in the extremities (the sciatic nerve). In specimens obtained from patients with severe, generalized arteriosclerosis, the peripheral nerve was found to be a site of severe pathological changes whereas changes were moderate in the Schwann part of the sympathetic nerves and in the vagus nerve.

The arteriosclerotic lesions in extra-cranial nerves have been described in greater detail, for instance by *Cottrell* (1940), *Eames and Lange* (1967), and *Ochoa and Mair* (1969).

Author's studies and results

In 33 temporal bones out of 43, intraneural vessels of the vestibulo-cochlear nerve were filled to a degree sufficient to allow a judgement of the vascular pattern. Ves-

sels were in all cases filled with "Microphil" or with a grained dye material suspended in 10 % gelatine. In the remaining 10 cases, vessels in the acoustic nerves were either insufficiently filled (six out of the 10) or they had been reproduced by staining of the vascular walls, using alkaline phosphatase reagent (four out of the 10). It proved impossible to judge the pattern on the basis of freeze-sections of the acoustic nerve and consequently these specimens are not included in the final survey.

In 24 out of the 33 specimens studied, injections managed to fill the Schwann part as well as the glial part of nerves. Filling was optimum in the Schwann part in all cases. In the remaining nine specimens, satisfactory filling was obtained only in one of the two parts. In two out of these 24 specimens, two dye materials were used for the reproduction of the intraneural vessels; they were injected via the anterior inferior cerebellar branches and carotid branches, respectively. Both dye materials coincided in one and the same vascular segment within all zones of these nerves.

Dye materials injected via anterior inferior cerebellar branches were seen to penetrate into the intraneural branches, either via branches arising from this main stem or via branches from the internal auditory arteries; finally, filling via vessels which united the dura in the internal auditory canal with the epineurium also was achieved.

The vascular pattern, calibres of vessels, and vascular density in the Schwann part seemed to be uniform, no matter the age of patients. The pattern might appear in the form of rectangular loops composed of longitudinal vessels of arteriolar calibre, or pre-capillary calibre; they were also seen to be composed of the interspersed transverse vessels. If counted over the diameter of nerves, an average of 15 to 20 such "meshes" would be in evidence.

The vascular density is considered to be identical at axial sites and at the more superficial sites in the Schwann part, no matter the age of patients. The nerve arises from the modiolus, emerging through tractus spiralis foraminosus, at which site an apparently high number of vessels is seen to enter into and emerge from the basal coil superficially in the nerve; this was true even in specimens originating from old patients with generalized arteriosclerosis.

In the glial parts of nerves, i.e. in the transitional zone as well as in more centrally situated zones, nothing but longitudinal vessels were in evidence as it had proved impossible to apply injections into transverse vessels. Such longitudinal vessels are often direct continuations of those in the Schwann part.

Two nerves belonging in this series, i.e. those in which filling of the vascular system was optimum, were re-embedded in celloidine and cut into serial sections measuring 7 micron; additional staining included haematoxylin-PAS. In similarity with findings in the thick, cleared sections, vascularization seemed to be most dense in the Schwann part. Furthermore, the vascular density at axial and peripheral sites seemed to be identical in all parts of the nerves.

Owing to the deficient filling in glial parts of the nerves it might be difficult to determine the ratio of numbers of vessels in patients in one age group to numbers of vessels in patients in other age groups.

At the line of demarcation between the Schwann part and the glial zone of transition, the vascular pattern changed abruptly from the type observed in the Schwann part into that seen in the glial parts. This feature was observed in nerves from patients in all age groups.

Discussion and conclusion

The vascular density throughout the Schwann part of the 8th cerebral nerve was found to be uniform in all specimens, no matter the age of patients. This is in conformity with the findings obtained by *Takahashi* (1966) in a study of the vagus nerve and the sympathetic nerves.

The apparently large number of vessels to pass through that part of tractus spiralis foraminosus which leads to structures in the basal cochlear coil is not commensurate with data submitted by *Krmpotić* (1969) who declared that the foramina in tractus spiralis foraminosus would occlude late in life; according to this author, a strangulation of vessels and nerves entering into the structures of the basal cochlear coil might thus be one of the factors responsible for the development of presbycusis.

The abrupt shifting from the dense and regular vascular patterns in the Schwann part to the less dense pattern, or rather a vascular system into which injection had been more sparse, seen in the transitional zone and other zones in the glial nerve, is in agreement with findings obtained by *Němecěk et al.* (1969).

As regards the severity of the degenerative changes, it should be mentioned that a similar abrupt shifting at the line of demarcation between the Schwann part and the glial part of the 8th cranial nerve has been observed in patients with generalized arteriosclerosis involving the main ramifications of the anterior inferior cerebellar artery in the internal auditory canal (patients in group I, chapter IV); in these patients, the lesions involving the Schwann part were found to range between mild and moderate degrees whereas changes in the glial parts of the nerve were considered to be severe, even monstrous (approximately like those observed in the white matter of the cerebral hemispheres) (*Hansen and Reske-Nielsen*, 1965).

CHAPTER X

Summary and Discussion of Clinical and Anatomical Findings

The clinical findings together with the patho-anatomical and normo-anatomical studies are summed up and discussed in chapter X. The object of the study has been to illustrate, even to define if possible, the aetiology involved in certain types of perceptive hearing loss, particularly that to develop late in life.

Re Part I

Temporal bones and brains from 14 patients have been exposed to microscopic study; the histological findings have tentatively been correlated with those obtained by clinical and otological examination as well as by pure-tone audiometry.

Examination of the patient discussed in chapter II (abstract of treatise A: Cortical Hearing Loss in a Patient with Glioblastoma) shows that the hearing capacity may vary parallel with cerebral lesions exclusively; in the present case, oedema has been found to involve the cerebral hemispheres; moreover, the loss of hearing is found to be of the presbycusis type.

Chapter IV is an abstract of treatise B: Pathological Studies in Presbycusis. Cochlear and Central Findings in 12 Aged Patients. The following conclusion is drawn: In 11 of the patients, the loss of hearing applies to the high-frequency range as well as to the low-frequency range; the loss of hearing of tones in the high-frequency range seems to be attributable to lesions involving central as well as peripheral sites while the loss of hearing of tones in the low-frequency range seems to be due to lesions at cerebral sites exclusively, the apical and middle coils remaining intact in the latter cases or the pathological changes might be slight only. Among these 11 patients, the one in group IV is included though the lesion applies only to the right ear. The hearing loss of classic presbycusis type in one patient (group III) is explicable only as a consequence of changes affecting the acoustic nerves and the brain since the cochlea is found to remain normal in this patient.

In chapter V (abstract of treatise C: Pathological Studies in Perceptive Deafness. A Patient with Hydrops of the Labyrinth), a patient is discussed in whom Ménière's disease, arteriosclerosis, and loss of hearing of tones of all frequencies are diagnosed. The hearing loss may have been due to pathological processes at peripheral as well as central sites.

Distribution of the pathological processes involving the cochlea and the cerebrum varies greatly from patient to patient; this seems particularly notable in the cases of patients suffering from presbycusis in whom the cochlear structures remain either intact or slightly to moderately altered as compared with the often severe

cerebral lesions. Intracranial vascular changes, including those involving the basilar circulation and vessels in the internal auditory canal seem also to be extremely severe while structures in the peripheral auditory organ are well-preserved.

Inspired by the results thus obtained, the author embarked upon an experimental study of vessels in order to examine whether the relative integrity of intralabyrinthine structures might be maintained by hitherto unrecognized vessels in excess of the branches of the intracranial vascular system.

Re Part 2

In 43 temporal bones obtained from 33 individuals, the vascular system has been filled to various degrees by means of a micro-injection method elaborated by the author. The composition of the material is very heterogeneous both as regards the distribution according to age of patients and the media used for injections; also the sites of injections vary, the media being applied either via extra- or intra-cranial vessels. The techniques used for injection and dissection are described in detail in chapter VI (the description of the method used for injection is an abstract of that previously published in treatise D: Vascular Anatomy of the Human Temporal Bone. A Preliminary Report).

Coincident microscopy of the equivalent brains and injections into these have not been possible. Gross inspection of brains from these old patients, however, might often disclose severe, mostly sporadic, vascular changes. Severe arteriosclerotic changes were also seen to involve the basilar vessels. Intracranial vessels supplying right and left temporal bones were found to deviate greatly in calibres and morphology.

In chapter VII (abstract of treatise E: Vascular Anatomy of the Human Temporal Bone. I. Anastomoses between the Membranous Labyrinth and its Bony Capsule) the vascular communication between the cochlea and the otic capsule is described; such communications are filled with the above mentioned contrast media. In all temporal bones where the contrast media are seen to penetrate to the loosely built bone shelf between the basal and middle cochlear coils (31 bones), vascular anastomoses of arteriolar calibre are found to unite the modiolus with the vascular system in the enchondral layer of the otic capsule. This feature is demonstrable whether injections are applied via basilar vessels or carotid branches. Furthermore, vessels of calibres paralleling those of radiating arterioles of the vestibular scale are demonstrable in 15 specimens; these vessels arise at right angles to the latter and, transversing the endosteal layer, they unite with the vascular system of the enchondral layer. The phenomenon is seen in all of the cochlear coils. Moreover, in 14 specimens the contrast media are seen to penetrate between fibrils of the endosteal layer.

By this means it is demonstrated that *the cochlear vessels are no end-arteries*. Vascular communication between the otic capsule and the intracochlear structures is apparently especially abundant at the level of the basal coil, including the vascular network around its spiral ganglion. In this cochlear region, communica-

tions to four vascular branches are established, namely to the spiral modiolar artery, to the cochlear branch of the vestibulo-cochlear artery, to intraneural vessels of the auditory nerve, as well as to vessels to and from the enchondral layer of the otic capsule. At apical sites of the modiolus, however, vascular communication is in evidence only to the spiral modiolar artery and the intraneural vessels of the auditory nerve.

The abundant injections into the basal coil include also the vascular system of the basilar membrane, even the vessel of the basilar membrane. This feature is observed also in temporal bones derived from old patients in whom osmic acid staining of the organ of Corti discloses a coincident disappearance of hair cells there. In one such specimen it is even possible to trace grained contrast media between vessels in the basilar membrane and the vascular stria via vascular communications within Reissner's membrane at the site of the basal coil.

The further course of the vascular anastomoses through the other structures of the temporal bone is discussed in chapter VIII (abstract of treatise F: Vascular Anatomy of the Human Temporal Bone. II. Vascular Anastomoses inside the Labyrinthine Capsule). It is attempted to have vessels in the otic capsule filled via basilar vessels (41 specimens), carotid vessels (10 specimens), and via both in one and the same temporal bone (8 specimens). The degrees of filling vary although variations are not dependent on ages of patients or types of grained contrast media applied.

By means of such injections it is possible in 16 specimens to follow vessels in their courses between the internal ear and the middle ear throughout two or three layers of the otic capsule. In addition, direct communication between carotid vessels and basilar artery branches might be demonstrable by injections into either one of these areas, or into both within one and the same temporal bone. In two cases, such communications are demonstrable within the cochlea where the dye materials appear in one and the same intracochlear vessel which might be one in the modiolus, in the basilar membrane, or in the vascular stria. Double-injections of this type also disclose anastomoses between separate anterior inferior cerebellar branches (the subarcuate artery and the internal auditory artery) in the bone substance *per se*. Arterio-venous anastomoses of arteriolar calibre are also found to unite the inferior petrosal sinus with the arterial system. Such arterio-venous anastomoses of smaller calibres are seen to unite the vascular area of the subarcuate artery with the superior petrosal sinus.

Certain areas of the osseous labyrinthine capsule which during foetal life are the sites of the most abundant penetration by connective tissue and vessels are seen to be particularly well-filled with dye materials; these areas are the following: the area round about the semicircular canals, particularly well-filled via the subarcuate artery branches; the area between the base of the cochlea (including the osseous shelf wedged in between the middle and the basal coil), the vestibule, the fundus of the internal auditory canal, and the middle ear promontorium, particularly well-filled via the internal auditory artery branches. The latter area is termed "the vascular key area" by the present author, while the same region is termed Cozzolino's zone according to *Eckert-Möbius* (1926).

Finally, the vascular pattern in the vestibulo-cochlear nerve is studied in this series of temporal bones to which injections are applied. The study is described in chapter IX (abstract of treatise F: Vascular Anatomy of the Human Temporal Bone. III. The Vascularization of the Vestibulo-Cochlear Nerve). In the peripheral part, the Schwann part, of the nerve (the term referring to the presence of Schwann's supporting cells), the vascular pattern is found to be perfectly normal in patients in all age groups.

The vascular pattern is seen to change distinctly at the site of transition between the Schwann part and the glial parts of the nerve (termed according to the different types of supporting cells involved). Vascularization seems to be less rich in the glial than in the Schwann part. The same is noticed in two well-filled nerves cut into serial sections of a thickness of 7 micron and stained with haematoxylin-PAS. The vascular density in peripheral and axial parts of the nerves is apparently equal.

Discussion

The cited literature and the most essential results obtained in the present study have formed the basis of a discussion of the aetiology involved in perceptive deafness diagnosed in the patients comprised in the author's series.

It is attempted to evaluate and compare degrees of severity of the pathological processes involving the temporal bones and brains of the patients discussed in Part 1. The findings obtained suggest that the loss of hearing is attributable mainly to the cerebral lesions.

In patients in whom the degree of deafness of the presbycusis type "pertaining to age", the most severe lesions are found to involve the white matter of the cerebral hemispheres together with the glial part of the acoustic nerve (three patients in group I, one in group II, chapter IV (table 1, page 28)).

In two cases the hearing losses are of degrees beyond that "pertaining to age" while the audiometric curves are found to be of the typical presbycusis shape; in one of these patients in whom the peripheral auditory organ is intact, the most severe pathological processes involve the cerebral hemispheres (cf. chapter II; the data are obtained during periods when involvement of both cerebral hemispheres is manifest in the patient concerned); lesions in the other patient (group II, chapter IV (cf. table 1)) are found to involve the cerebral hemispheres and the acoustic nerves while the cochlea are seen to remain intact.

The loss of hearing applying to the high-frequency range is in three patients found to exceed the level otherwise encountered in cases of presbycusis (two patients in group I, one in group II, chapter IV (cf. table 1)). The cerebral lesions are in all cases considered to be much more severe than those observed in the peripheral auditory organs. Besides, the cochlear changes are found to be of the same degree as those observed in cases where curves suggest presbycusis. Thus the hearing loss applying to the high-frequency range and exceeding that otherwise considered typical of old age, is assumed to be attributable mainly to the cerebral lesions.

The hearing loss applying to the low-frequency range is in five patients found to exceed the level otherwise encountered in cases of presbycusis (three patients in group I, one in group IV (cf. table 1)); the fifth patient who is discussed in chapter V was suffering from Ménière's disease. It is rather difficult to decide whether a parallel can be drawn between the degree of the loss of hearing of tones in the low-frequency range and the severity of the pathological processes involving any specific site in the cerebral auditory pathways and centres. It is concluded, however, that such loss of hearing of tones in the low-frequency range mainly, if not exclusively, may be attributable to cerebral lesions in these senile patients (cf. chapter IV) in whom nothing but insignificant degenerative lesions are seen to involve structures of the middle and apical coils, even though degrees of such deafness may vary considerably. As regards the patient with Ménière's disease (chapter V), the histological findings suggest that the hearing loss applying to the low-frequency range might be attributable in part to the cerebral lesions.

Other investigators, for instance *Jørgensen* (1961) and *Ishii* (1967) have also observed such heterogeneous distribution of arteriosclerotic, vascular, degenerative changes including the involvement of intracranial vessels and vessels in the internal auditory canal in cases in which the cochlear vessels are only moderately affected.

On the other hand, the degrees of degenerative changes in cochlear as well as cerebral neural elements have not been described before. A few authors, namely *Matzker* (1958) and *Kirikae* (1964), observed disappearance and degeneration of cells in the auditory pathways and centres of the brain stem.

In some of the patients discussed in Part 1, a distinct line of demarcation was seen to distinguish between the severe, even monstrous, changes involving the central neural elements and the moderate changes at peripheral sites, namely at the site of transition from the glial part to the Schwann part of the acoustic nerve within the internal auditory canal. *Takahashi* (1966) observed similar features in the intracranial nerves of patients with severe, generalized arteriosclerosis. Morphological studies by *Němecěk et al.* (1969) disclosed an equally distinct line of demarcation at the identical site in the 1st neurone of the auditory pathways; in addition, these authors found that vascularization pertaining to the peripheral Schwann part was strikingly richer than that in the glial part of the 8th nerve.

On the basis of the experimental injections described in Part 2, the author estimates that the vascular pattern is most dense within the Schwann part of the acoustic nerve; this applies even to findings in old patients.

Likewise, it emerged that the cochlea is in vascular communication with the surrounding bone structures and, in fact, is not isolated from the latter. The intracochlear structures in all coils, but mainly those in basal coils, are actually in vascular communication with extracranial areas via anastomoses of arteriolar calibre. The latter is demonstrated by injections via intra- and extra-cranial vessels as well as by coincident injections via both into temporal bones from patients in all age groups.

The fact that intracochlear structures remain well-preserved even in patients

with severe arteriosclerosis may find its explanation in this additional vascular supply to the cochlea. This opinion is formed on the basis of aa pooling of vessels into which grained contrast media is applied and of vessels reproduced by means of osmic acid perfusion. Such additional supply serves also to explain why degeneration in the right and left cochleae is symmetrical in patients with presbycusis, irrespective of the marked asymmetry of vessels at the base of the brain and the uneven distribution of arteriosclerotic plaques in this vascular region. The asymmetry of vessels in the basilar system has been demonstrated by *Levin* (1964) and by the present author (chapter VI).

This additional vascular supply to the cochlea suggests that bone anastomoses are of value for the nutrition of the cochlea, even in very old individuals, because the apparently dense vascular network in temporal bones from the latter are satisfactorily filled. Owing to the heterogeneity of the material as regards media used for injections, sites to which injections are applied, and also the varying degrees of filling in vessels in patients in the individual age groups, it is hardly possible to draw any conclusions concerning the number of vessels which, in patients in the individual age groups, may be suitable for injection.

It appears from the literature, however, that the rate of metabolism in bone structures of the temporal bone remains almost unchanged throughout life (*Zechner and Altmann*, 1969) and also that the vascular supply is only moderately affected by arteriosclerosis in old patients (*Gussen*, 1968). Even so, the latter author found thrombi to be numerous in vessels in individuals in whom the severity of generalized arteriosclerosis, measured by their age, was abnormal (*Gussen*, 1969).

The intracochlear changes observed in the patients discussed in Part 1 are manifest mainly in the form of varying degrees of disappearance and degeneration of ganglion cells at the level of the basal cochlear coil. Any proportionality between degrees of these pathological changes and hearing losses diagnosed is not demonstrable. In patients with presbycusis, for instance, apparently normal conditions (patient no. 6, chapter IV) may alternate with a disappearance of about 75 % of the cells in other patients. In two patients whose hearing losses of the presbycusis type are of a severity otherwise observed in much older patients, conditions seem to be normal (patient no. 11, group III, chapter IV and the patient discussed in chapter II whose hearing impairment occurred during periods when bilateral hemispherical changes were manifest).

This discrepancy between degrees of severity of the pathological processes and the diagnosed hearing losses has been described also by *Crowe et al.* (1934); *Saxén* (1952); *Fleischer* (1956); and *Jørgensen* (1961).

By means of the vascular injections described in Part 2, it is possible to demonstrate that vessels communicating with the capillary plexus surrounding the spiral cochlear ganglion are most numerous at the site of the basal coil. Vessels in direct communication with the otic capsule (chapter VII) and further progressing to extracranial areas belong to this category (chapter VIII). Taking into consideration

that this feature is demonstrable in temporal bones from patients in all age groups, it seems rather paradoxical that the ganglion cells in the basal coil are the ones which are prone to disappear and degenerate. One reason may be that metabolic waste products might accumulate mainly at this site where the blood supply is most profuse; the latter postulation is substantiated by the fact that hearing losses in old individuals are found to be attributable to nutritional factors (*Rosen and Olin*, 1965). Another explanation is suggested by *Meyer zum Gottesberge et al.* (1965) and *Rauch* (1967) according to whom the energy consumption is highest in the basal cochlear coil where also wear and tear is most marked, as demonstrated by *von Békésy* (1960) who observed that all tones would produce vibrations in the basal cochlear coil whereas the apical cochlear coils are activated exclusively by tones in the low-frequency range.

It remains open to discussion whether lesions of ganglion cells in the basal cochlear coil are contributory to the hearing losses observed in patients in the various series; in fact, *Crowe et al.* (1934), *Schuknecht* (1955), and *Citron et al.* (1963) declared that the hearing capacity may remain intact even though 50–80 % of the ganglion cells are destroyed. It should finally be emphasized again that the hearing loss of the presbycusis type diagnosed in one patient (chapter II) seems to be attributable almost exclusively to pathological processes involving the cerebral hemispheres.

The lesions in the organ of Corti (Part 1) are probably artefacts which may have developed after death; in the present study, similar lesions were demonstrable in osmic acid stained preparations from old individuals (cf. Part 2); such staining served to reveal the disappearance of hair cells at the site of the basal coil; this feature is in conformity with findings obtained by *Bredberg* (1968). Furthermore, coincident injections of dye material into these specimens are seen to fill vessels in close connection with the organ of Corti, even in the region of the basal coil (Part 2, chapter VII). This is in conformity with findings obtained by *Axelson and Ernstsson* (1970) in experiments with waltzing guinea pigs in which injections were applied into the vessel of the basilar membrane.

So far, it cannot be decided whether the demonstrated lesions in the organ of Corti may have contributed to the loss of hearing in the patients here discussed; in fact, the histological findings may not have been of any consequence. *Ruben* (1963) found the cochlear microphonic potential to be normal in an old patient with presbycusis. Also *Schnieder and Janzer* (1969) who exposed guinea pigs to histochemical analysis and, in addition, measured the cochlear microphonic potential as a standard of the degenerative changes to develop in the organ of Corti, found such functional measurement out of proportion to the histologically demonstrable changes induced by "white noise".

All cochlear vessels in the patients discussed in Part 1 seem to remain relatively well-preserved; also temporal bone vessels from the same sites (discussed in Part 2) are suitable for injection, no matter the age of patients.

Furthermore, the injection experiments provide evidence of a vascular communication between the vascular stria and the basilar membrane, namely via Reissner's membrane.

Atrophy of the vascular stria like that observed by *Schuknecht* (1955) and *Ishii* (1967) in senile patients is not encountered in any of the patients discussed in Part 1. Indeed, the vascular stria is found to be well-filled in temporal bones removed from old patients (Part 2).

Conclusion

According to the histological analysis of structures in temporal bones and brains in patients with various types of perceptive hearing impairments, such impairments as apply to the high-frequency range seem to be attributable, at least partly, to lesions involving cerebral sites whereas impairments applying to the low-frequency range apparently are due to cerebral lesions exclusively. Only the patient with Ménière's disease represents an exception.

Examinations of temporal bones to which contrast media are applied seem to substantiate the hypothesis according to which arteries in the peripheral auditory organ are not end-arteries; in fact, it applies to individuals in alle age groups that the cochlear vessels are found to communicate with intracranial as well as extracranial sources. The latter feature may explain why structures of the internal ear are found to be relatively well-preserved in elderly patients (Part 1) in spite of the severe neurogenic and vascular anomalies encountered at the more centrally localized sites in the auditory pathways.

As regards the intracochlear structures it must be admitted that there is a certain discrepancy between the particularly rich vascular supply to the basal cochlear coil and the rather severe degenerative lesions to develop within the same region. As to the vascular supply to the middle cochlear scale, it should be stressed that grained contrast media are seen to penetrate right into the vessel of the basilar membrane, vessels being well-filled even in areas where coincident disappearance of hair cells in the organ of Corti is in evidence. Furthermore, these vascular injections serve to demonstrate the vascular communication between the basilar membrane and the vascular stria, via Reissner's membrane.

Thus, by way of a comparison of findings in ears and brains (Part 1) and by means of experimental injections into vessels of the temporal bone (Part 2), perceptive hearing impairments, including the so-called "hearing loss pertaining to age" is found to be mainly attributable to the pathological processes at intracranial sites.

Continued research in the fields of audiology and pathology, including studies of all parts of the complicated auditory system, is urgently required. Such research should include examination of all structures within the temporal bones, including the otic capsule. In this connection, the attention shall be directed to the technique used for such injections, a technique which has been improved and elaborated by

the author; this technique is combined with the generally accepted methods hitherto used in phase-contrast microscopy and in routine histological procedures. It is recommended to use thick, cleared sections, as described in the present study, including cutting into thinner sections and additional staining according to conventional histological methods.

The technique may prove valuable whenever specific problems are to be solved, for instance, problems involved in a definition of the factors responsible for the acutely developing hearing losses. On the assumption that the vascular anastomoses here described contribute to the preservation of a certain integrity of structures in the internal ear in patients of this category, it may be taken into consideration to institute oto-neurosurgical measures by which to counteract the defect. Moreover, comparative studies of temporal bones and cerebral structures in patients exposed to several audiological tests seem to be of importance for the establishment of more advanced neuro-otological diagnostics.

SUMMARY

In the present monograph, including clinical examinations and studies of the normal anatomy as well as the patho-anatomical features involved, it is attempted to detect the factors responsible for the development of the various types of perceptive hearing loss, in particular those responsible for the development of deafness termed "hearing loss pertaining to age".

The monograph comprises two parts:

Part 1: Histological studies of temporal bones and brains from patients with diagnosed hearing loss of perception type (chapters I–V).

Part 2. Experiments including injection of contrast media into the vascular system in temporal bones from man (chapters VI–X).

Chapter I. The material is described and the methods used for dissection of specimens and histological staining of temporal bones and brains are discussed.

Chapter II. The lesions observed in a 43-year-old patient are discussed. His hearing was found to be normal, but a glioblastoma was seen to involve one cerebral hemisphere. Audiometry performed twice during two periods in which cerebral oedema, provoked by the surgical treatment of the tumour, was manifest, revealed on both occasions a symmetrical loss of hearing, applying mainly to tones in the high-frequency range; on both occasions, audition paralleled that which, according to the literature, otherwise is seen in normal, 75-year-old patients. The last episode of cerebral oedema terminated in the sudden death of the patient. On the basis of histopathological analysis of the brain and of the apparently normal left temporal bone, the following conclusion is drawn: Throughout the periods in which the pathological changes provoked by the tumour involved exclusively the right cerebral hemisphere and the right side of the brain stem, with the exception of the trapezoid body, audition remained normal in this patient while a hearing loss of the presbycusis type occurred during the two episodes of surgically excited cerebral oedema; these episodes were associated with *extinct action of the left cerebral hemisphere*. In other words, audition is found to fluctuate parallel with pathological lesions involving the cerebrum.

Chapter III comprises a review of previously published works in which the hearing capacity of senile patients is collated with findings obtained by histological studies of isolated parts of the auditory pathways, for instance, single sites in the temporal bone or in the brain.

Some authors have studied the peripheral auditory organ and concluded that pathological lesions at that site were not sufficient to explain the development of the diagnosed hearing loss; consequently they suggested that cerebral lesions might be responsible in part, particularly in cases in which the hearing loss applied to tones in the low-frequency range.

The attention is directed also to a few reports according to which degeneration of the acoustic nuclei in the brain stem had been demonstrable.

Studies are not available, however, in which the peripheral as well as the cerebral neurones have been examined in patients whose hearing loss developed late in life.

Chapter IV. The series discussed comprises 12 senile patients who all except one were above the age of 65 years. The cerebral auditory pathways, the auditory nuclei in brain stem and cerebral hemispheres, as well as the right and left temporal bones were studied in these patients. In one patient, examination applies only to the right ear.

In 11 of the patients, the hearing loss of tones in the high-frequency range is apparently due to cerebral as well as peripheral lesions; the loss of hearing of tones in the low-frequency range seems to be attributable exclusively to cerebral lesions since the apical and middle coils remain normal, or only slightly damaged. In one of these 11 patients (the one in group IV), only the right-sided hearing loss could be explained, as mentioned above. In one patient (the one in group III), the loss of hearing of tones in the high-frequency range is explicable exclusively as a consequence of the lesions involving the acoustic nerve and the brain stem since the cochleae on either side remain of normal appearance.

Chapter V. The past medical history of an 83-year-old patient with Ménière's disease is reviewed. The pathological changes involving the temporal bones and the brain are discussed.

The bilateral labyrinthine hydrops can hardly be held solely responsible for the hearing loss; in particular it cannot be held responsible for her hearing loss applying to tones in the low-frequency range, taking into consideration that the labyrinthine hydrops involved mainly the right ear on which audition was best preserved. Furthermore, the lesions involving the 1st neurone in the acoustic pathways, mostly lesions apically in the cochlea, are not sufficient to explain a loss of hearing of tones in any range; on the other hand, disappearance and degeneration of cells are by far more marked in the acoustic nuclei and auditory pathways in the brain and hence, the hearing impairment must be considered attributable to cerebral as well as to peripheral lesions, whether the hearing loss applies to tones in the low- or high-frequency range.

In contrast, the impairment of the vestibular function is apparently attributable exclusively to cerebral lesions since there is a clear-cut discrepancy between the severely reduced caloric reactions in both ears and the normal aspect of the vestibular labyrinth, including the 1st neurone, coincident with the extremely severe lesions of the vestibular nuclei and pathways in the brain stem.

Chapter VI. The composition of the material (discussed in Part 2) is described together with the methods used for removal of specimens, experimental injections, and dissection of the 43 temporal bones derived from patients in all age groups. On the basis of this material it is endeavoured to explain some of the patho-anatomical findings discussed in Part 1.

Chapter VII is concerned with the vascular communication between the membranous labyrinth and its otic capsule; also the pattern of filling obtained in certain areas of the cochlear vascular system is described.

In all temporal bones in which the contrast media appear at the site of the basal cochlear coil in the modiolar vessels (a total of 31), the media are seen to penetrate directly into the enchondral layer of the otic capsule, namely via the osseous shelf separating the basal coil from the middle coil. Arterial- as well as venous anastomoses between extra- and intra-labyrinthine vessels are in evidence. In addition, vascular communications traversing the endosteal layer are found to unite the intracochlear vascular network with vessels of the enchondral layer. This feature is demonstrable in all cochlear coils. Such communication is mediated either via canaliculi of capillary calibres interspersed among the osseous fibrils in the endosteal layer *per se*, or via arterioles arising from the radiating arterioles of the vestibular scale. Anastomoses of these types are demonstrable in all temporal bones, no matter the age of individuals from whom they are derived; in the present series they are encountered in one 5-day-old infant as well as in patients above the age of 90 years. The various types of vascular anastomoses can all be filled by injections of contrast media via intra- as well as extra-cranial vessels known to supply temporal bones. Accordingly, *the intralabyrinthine arteries are no end-arteries*.

The intracochlear vascular supply seems to be most abundant at the site of basilar coil structures, especially at the vascular network surrounding the spiral ganglion. Furthermore, vessels in the basilar membrane seem to be well-filled, irrespective of the severity of the degenerative changes involving the organ of Corti, visualized by staining with osmic acid. Vessels uniting the vascular stria with the basilar membrane vessels, via Reissner's membrane, are also in evidence.

Chapter VIII. The vascular pattern of the otic capsule, reproduced by injections into temporal bones, is described; the specimens are the same as those discussed in chapter VII. The enchondral layer seems to be especially well-provided with vessels; this feature is apparent from the injection pattern in temporal bones from patients in all age groups. This layer can be filled through extra- as well as intra-cranial arteries. Injections via both sources in one and the same specimen disclose end-to-end anastomoses of arteriolar calibres between these. Furthermore, such duplicate injections reveal the presence of arterio-venous anastomoses which also are of arteriolar calibres.

As regards the osseous regions of the osseous capsule, filling is most satisfactory in: (a) the region medially to the subarcuate fossa, mainly supplied from the intracranial vessels via the subarcuate arterial branches; (b) the osseous region

which antero-posteriorly separates the vestibule from the cochlea, including the osseous shelf between the basal and the middle coils and which medio-laterally separates the middle ear promontory from the internal auditory canal.

Throughout this vascular system, and in all layers of the otic capsule, it is possible to follow the unintermittent course of vessels of arteriolar calibre between the intracochlear structures and distant structures such as the promontory of the middle ear and the internal carotid artery in its course through the carotid canal.

Chapter IX. The vascular supply to the acoustic nerve is described. It applies to all age groups that the vascular system in the Schwann part of nerves is richer and more regular than that in the glial parts. In the internal auditory canal, the transition between the two patterns produced by injections is clear-cut.

Chapter X. The subject matter of this chapter is a synoptic conclusion and discussion of the findings described in Parts 1 and 2.

Part 1. By means of the available methods for light microscopy, the degenerative lesions of labyrinthine structures in 14 patients with various types of hearing losses, mainly of the presbycusis type, are found to be less marked than those involving cerebral auditory pathways and centres. In fact, in two patients with presbycusis, the peripheral hearing organ is apparently normal. The Schwann part of the acoustic nerve seems to be well-preserved despite the severe arteriosclerotic lesions of vessels passing through the internal auditory canal at extraneural sites; conversely, degeneration in the glial part of nerves is of a degree similar to that involving the white matter of the cerebral hemispheres. As regards the cochlea, the only pathological changes other than those attributable to autolysis, include disappearance and degeneration of ganglion cells at the site of the basal coil of the spiral ganglion, although it must be admitted that the feature is not proportional to the diagnosed loss of hearing of tones in the high-frequency range.

Thus, the conclusion must be that the factor or factors responsible for the diagnosed losses of hearing are such lesions as involve central as well as peripheral sites in the auditory system; two of the patients in whom hearing curves were of presbycusis type represent the exception to this rule, their hearing losses being attributable to cerebral lesions exclusively.

Part 2. The results obtained by experimental injections into vessels of 43 human temporal bones derived from patients in all age groups are submitted in part 2. The purpose of such injections is to provide an explanation of the above mentioned findings in temporal bones from the patients discussed in Part 1.

It is demonstrated that the cochlear arteries are not end-arteries, rather they are seen to unite with vessels in the otic capsule, particularly at the site of the basal cochlear coil, extending further to structures of the middle ear, finally to unite directly with carotid branches. Accordingly, the cochlea can be filled also via injections into carotid branches. Such anastomoses are demonstrable in temporal bones, no matter the age of individuals from whom they are removed; the otic capsule is also found to be well-filled with contrast media, even in specimens derived from old patients with severe, generalized arteriosclerosis. The demon-

strable blood supply via the otic capsule serves to explain the observation of well-preserved cochlear structures of the middle and apical coils in old patients. On the other hand, these injections fail to explain why structures of the basal cochlear coil have degenerated, taking into consideration that vascular anastomoses, via the otic capsule, to this part of the cochlea are found to be particularly abundant. Injections of contrast media fail to provide an explanation of the degenerative changes to be observed by means of osmic acid staining of the organ of Corti and seen to involve the basal cochlear coil in temporal bones from senile patients with generalized arteriosclerosis. In these cases the contrast media are seen to penetrate even into the vessel of the basilar membrane.

RESUMÉ

I det forelagte arbejde er det forsøgt ved hjælp af kliniske undersøgelser og normal-anatomiske såvel som patologisk-anatomiske studier at undersøge årsagerne til forskellige former for perceptionshøretab – specielt det såkaldte »aldersbetingede« høretab.

Arbejdet er inddelt i 2 afsnit:

1: Histologiske studier af tindingeben og hjerner fra patienter med kendte perceptionshøretab (kapitel I–V).

2: Experimentelle kontraststofinjectioner af karsystemet i humane tindingeben (kapitel VI–X).

Kapitel I indeholder en beskrivelse af materialet og af de metoder, der er brugt ved udtagning og farvning af det histologiske materiale omfattende tindingeben og hjerne.

Kapitel II. En 43-årig patient med normal hørelse er fulgt audiometrisk i 2 perioder hvor hjerneødem optrådte efter operative indgreb mod tumor; i begge perioder fandtes symmetriske høretab, specielt i højfrekvensområdet, svarende til hørelsen man, ifølge litteraturen, møder hos 75-årige patienter. Patienten døde pludseligt i tilslutning til sidste hjerneødemperiode. Ud fra en histopatologisk analyse af hjerne og af venstre os temporale, der findes normale, konkluderes følgende: I perioderne, hvor de patologiske forandringer forårsaget af tumor begrænser sig til h. cerebrale hemisfære og h. side af hjernestammen bortset fra corpus trapezoideum, er hørelsen normal. Under de to perioder med diffust hjerneødem i forbindelse med operationerne, hvor også *venstre* hemisfære delvis er sat ud af spillet, har patienten det presbyacusic lignende høretab. Det vil sige, at hørelsen fluctuerer med de skiftende patologiske tilstande i storhjernen.

Kapitel III omfatter en summarisk gennemgang af tidligere publicerede arbejder, hvor forfatterne sammenholder hørelsen hos senile patienter med de histologiske fund i eet enkelt afsnit af hørebanerne, enten i os temporale eller i hjernen.

Enkelte forfattere, der har undersøgt det perifere høreorgan konkluderer, at de patologiske forandringer her, ikke er tilstrækkelige til at forklare de fundne høretab, hvorfor cerebrale forandringer må have spillet en rolle, specielt for lavfrekvenshøretabenes vedkommende.

Desuden refereres et par meddelelser vedrørende undersøgelser af de akustiske kerner i hjernestammen, der fandtes degenererede.

I intet arbejde er såvel perifere som cerebrale neuroner undersøgt hos patienter med høretab opstået i seniet.

Kapitel IV. Hos 12 senile patienter, hvoraf kun een er under 65 år, har man undersøgt cerebrale hørebaner og -kerner i hjernestammen og hemisfærerne såvel som begge perifere høreorganer, i eet tilfælde dog kun højresidige.

Hos de 11 patienter (hos 1 patient (gruppe IV) var kun højre øre impliceret), hvis høretab omfattede både høje og lave toner, synes højttonetabet at være centralt såvel som perifert betinget, mens lavtonetabet må være udelukkende centralt betinget idet de apicale og mellemste vindinger er normale eller kun let forandrede. Hos en enkelt patient (i gruppe III) kan høretabet, der er et højttonetab, kun forklares som et resultat af forandringerne i nervi acustici og hjernen, idet cochleae på begge sider er normale.

Kapitel V. Man gennemgår sygehistorie og patologiske fund i ossa temporalia og hjernen hos en 83-årig patient med morbus Ménière og arteriosclerose.

Den dobbeltsidige hydrops labyrinthii synes ikke at være eneste årsag til patientens høretab, specielt ikke til det tab der omfatter lavfrekvensområdet, da den er mest udtalt i grad og udstrækning i højre øre, hvor hørelsen er bedst bevaret. Tillige er de patologiske forandringer i 1. neuron af de akustiske baner ikke tilstrækkelige, specielt ikke de i den apicale del af cochlea, til at forklare en hørenedsættelse omfattende noget trin i frekvensområdet; derimod er udfald og degeneration langt mere udtalt i de akustiske kerner og -baner i cerebrum. Det anses derfor mest sandsynligt, at de akustiske udfaldssymptomer er centralt såvel som perifert betingede, hvadenten det gælder lav- eller højfrekvensområdet.

De vestibulære udfaldssymptomer synes derimod at være udelukkende centralt betingede, idet der er et åbenbart misforhold mellem den svært nedsatte kaloriske reaktion på begge ører og de tilsyneladende normalt udseende dele af labyrintherne, inclusive 1. neuron, samtidigt med at man ser overordentlig svære forandringer indenfor de vestibulære kerner og -baner i hjernestammen.

Kapitel VI omfatter en beskrivelse af materialet og af de metoder, der er benyttet ved udtagningen, de eksperimentelle karinjektioner, samt dissektionen af 43 tindingeben fra mennesker i alle aldersgrupper. Ud fra dette materiale har man forsøgt at finde en forklaring på visse af de patologisk-anatomiske forandringer, der omtales i afsnit 1.

I *Kapitel VII* omtales dels karforbindelserne mellem den membranøse labyrinth og dens otiske kapsel, dels fyldningsmønstret i visse områder af cochleas kar.

I alle tindingeben, i hvilke kontraststofferne fylder modioluskar svarende til basale cochleavinding (ialt 31), trænger kontrasten direkte ud i den otiske kapsels enchondrale lag via den løst strukturerede knoglehylde, der adskiller basale og mellemste vinding. Såvel arterielle som venøse anastomoser mellem ekstra- og intralabyrinthære kar kan påvises. I alle cochleavindinger findes kar der, gennem det endosteale lag, forbinder det intracochleære karnet og den otiske kapsels kar. Disse karforbindelser etableres dels via canaliculi af kapillærkaliber mellem selve det endosteale lags knoglefibriller, dels via arterioler, der udgår fra arteriolae rectae i scala vestibuli. Anastomoser af alle de nævnte typer kan demonstreres i tin-

dingeben fra patienter i alle aldersgrupper; de er set hos et 5 dage gammelt barn såvel som hos patienter over 90 år. De kan tillige fyldes ved injectioner i såvel intra- som ekstracranielle kar, der forsyner tindingebenet. *De intralabyrinthære arterier er således ikke endearterier.*

Intracochleært synes karforsyningen til basale vindings strukturer at være rigeligst, specielt i området omkring ganglion spirale cochleae. Endvidere ses god fyldning ud i membrana basilaris, uanset graden af de degenerative forandringer i det Cortiske organ, der kan iagttages ved hjælp af osmiumsyrefarvningerne. Der ses endvidere forbindelseskar mellem stria vascularis og membrana basilaris via membrana Reissneri.

Kapitel VIII. Karinjektionsmønstret i den otiske kapsel beskrives; tindingebens-materialet er det samme som det, der omtales i kapitel VII. Man ser i tindingeben fra patienter i alle aldersgrupper, at specielt det enchondrale lag er velforsynet med kar. Disse kar kan injiceres fra ekstra- såvel som intrakranielle arterier. Ved injektion fra begge karområder i samme præparat, kan der endvidere demonstreres end-to-end anastomoser af arteriolekaliber mellem disse. Ved sådan dobbeltinjektion findes endvidere arterio-venøse anastomoser af lignende kaliber.

De bedst fyldte knogleregioner er dels dem, der ligger medalt for fossa subarcuata, med tilløb af intrakranielle kar specielt fra a. subarcuata, dels det område, der anteriort-posteriort skiller vestibulum fra cochlea (indefattende knoglehylden mellem basale og mellemste vinding) samt, medalt-lateralt, canalis auditorius internus fra mellemørets promontorium.

Gennem dette karnet kan man følge kar, der fra intracochleære strukturer, ubrudt forløber gennem 2 eller 3 lag i den otiske kapsel til, blandt andet, mellemørets strukturer og carotiskar som f.eks. a. carotis interna i dens forløb gennem canalis caroticus.

Kapitel IX. Karforsyningen i nervus acusticus diskuteres. Det gælder for alle aldersgrupper, at karnettet er rigeligere og mere regelmæssigt i nervernes Schwanske del end i deres gliøse afsnit. Overgangen mellem de to injektionsmønstre i canalis auditorius synes skarp.

Kapitel X indeholder en sammenfattende konklusion og diskussion af de i afsnit 1 og 2 omtalte fund.

Afsnit I. Ved hjælp af de lysmikroskopiske metoder, der har været til rådighed har man skønnet, at de degenerative forandringer i labyrinthens strukturer er langt mindre udtalte end de forandringer, der er tilstede i hjernens hørebaner og centre hos 14 patienter med perceptionshøretab, specielt høretab af presbycusis-type. Det perifere høreorgan synes endog at være normalt hos to patienter med presbycusis. Den Schwannske del af nervi acustici er tilsyneladende velbevaret til trods for svære arteriosclerotiske forandringer i de kar, der passerer gennem canalis auditorius internus ekstraneuralt, hvorimod nervernes gliøse del ses at være degenereret i samme grad som den hvide substans i de cerebrale hemisfærer. I cochlea er udfald og degeneration af celler i ganglion spirale cochleas basale vinding det

eneste patologiske fund, der ikke synes at kunne tilskrives postmortelle forandringer, omend udfald og degeneration ikke er proportionale med de observerede højttonenhøretab.

Man må således konkludere, at årsagen, eller årsagerne, til de klinisk fundne høretab skal søges i såvel centrale som perifere afsnit af det auditive system; hos to af de her omtalte patienter med presbycusis syntes høretabet dog udelukkende cerebralt betinget.

Afsnit 2. Resultaterne af de eksperimentelle injektioner i kar i 43 tindingeben fra patienter i alle aldersgrupper beskrives med det formål at forklare de perifere læsioner, man har observeret hos de i afsnit 1 omtalte patienter. Det fremgår, at cochleas arterier ikke er endearterier, men at de forbinder sig med karrene i den otiske kapsel, specielt rigeligt svarende til basale cochleavinding, og videre ud til mellemørets strukturer, samt direkte til carotisgrene. Fyldning af cochleae kan således også ske ved injektion af carotisgrene. Disse anastomoser kan demonstreres i tindingeben fra patienter i alle aldersgrupper; i dette materiale blev også den otiske kapsel velfyldt med kontrast, selv i præparater fra gamle patienter med svær, universel arteriosclerose. Den således demonstrerede blodforsyning via den otiske kapsels kar kan derfor muligvis forklare, at man i det kliniske materiale omfattende gamle patienter (afsnit 1) finder velbevarede strukturer i mellemste og apicale cochleavindinger. Karinjektionerne forklarer derimod ikke hvorfor specielt basale cochleavindings strukturer er degenererede, idet karanastomoserne, via den otiske kapsel, til denne del af cochlea findes at være specielt rigelige. De degenerative forandringer man, ved osmiumsyrefarvning af det Cortiske organ, har kunnet finde i basale cochleavinding i tindingeben fra senile patienter med universel arteriosclerose, har heller ikke kunnet forklares ved kontrastofinjektionerne, idet kontrasten i disse tilfælde har udfyldt endog vas membranae basilaris i tindingeben fra disse.

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